IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Nicholas Bachynsky Woodie Roy	§	
	§	Group Art Unit: Unknown
Serial No.: 09/744622 (PCT/US99/16940)	§	
	§	Examiner: Unassigned
Filed: January 26, 2001	§	
	§	Atty. Docket: P01615US1 / 09805783
For: **CHEMICALLY INDUCED INTRACELLULAR HYPERTHERMIA**	§	(U.S. Nat'l. Phase)
	§	

Assistant Commissioner for Patents
BOX PCT
Washington, DC 20231
ATTN: PCT Legal Office

RENEWED PETITION UNDER 37 C.F.R. 1.47(B)

Dear Sir:

This Renewed Petition Under 37 C.F.R. § 1.47(b), is filed in response to a Decision on Petition dated 05 September 2002, for the above-referenced application, which dismissed the applicants Renewed Petition filed on 07 May 02, without prejudice. This Renewed Petition addresses issues raised by the PTO in the dismissal to the extent they were not addressed earlier. Applicants were given two months to file this Renewed Petition, subject to extensions under 37 C.F.R. § 1.136(a). The filing of this Renewed Petition Under 37 C.F.R. § 1.47(b), is timely because it is being filed prior to 05 December 2002, and within a one-month request for extension of time.

BACKGROUND OF PTO PROCEEDINGS

1. On 27 July 1999, applicants filed international application PCT/US99/1690, which claimed a priority date of 27 July 1998, based on a previously-filed provisional application. A copy of the international application was communicated to the United States

Patent and Trademark Office from the International Bureau on 10 February 2000. A Demand for international preliminary examination, in which the United States was elected, was filed on 23 February 2000.

2. On 26 January 2001, applicants filed a transmittal letter for entry into the national state in the United States. However, the applicant did not file an oath or declaration under 35 U.S.C.§ 371(c)(4) because the inventors refused to sign one.

3. On 05 March 2001, the United States Designated/Elected Office mailed applicants a "Notification of Missing Requirements Under 35 U.S.C. § 371 in the United States Designated/Elected Office" indicating that an oath or declaration in compliance with 37 C.F.R.§ 1.497(a) and (b) was required.

4. On 05 September 2001, applicants filed a Petition Under 37 C.F.R. § 1.47, and a declaration executed by the assignee on behalf of the non-signing inventors.

5. On 08 November 2001, the United States Patent and Trademark Office ("PTO") mailed a Decision Refusing Status Under 37 C.F.R. § 1.47, and dismissed the petition without prejudice.

6. On 07 May 2002, the applicants filed a Renewed Petition Under 37 CFR 1.47(B), along with supporting declarations and documents.

7. On 05 September 2002, the PTO dismissed the Renewed Petition without prejudice.

DEFICIENCIES NOTED IN 05 SEPTEMBER 02 DECISION

In its Decision of 05 September 2002, the PTO stated that the petition filed on 07 May 2002, was deficient for the following reasons:

- **Proof of Unavailability or Refusal** - Although the PTO found that applicant has shown that a bona fide attempt was made to present the application papers, including the specification, claims and drawings to Nicholas Bachynsky and Woodie Ray, it is unclear from the accompanying declaration whether the declarant G. Wayne Choate is basing his conclusion that the inventors refused the declarations on the actions of the missing inventors or if Mr. Choate is basing his

conclusions on conversations he had with the missing inventors or their counsel. The PTO noted that whenever the nonsigning inventor gives a reason for refusing to sign the application oath or declaration that reason should be stated in the petition. (Decision, p. 3)

- **Proof of Proprietary Interest** - Petitioner has not demonstrated that applicant has proprietary interest in the invention. Petitioner has provided an Assignment executed by Nicholas Bachynsky and Woodie Ray. As stated in the previous petition, the assignments of the "invention" were to Texas Pharmaceutical, Inc., show sufficient proprietary interest, however, those assignments are not acceptable to establish ownership and file the application under 37 CFR 1.47(b). The assignments do not identify the instant application by application number. (Decision, p. 4)

Applicants have corrected the deficiencies noted above, to the extent they were not satisfied in the earlier petitions, through the accompanying Supplemental Declaration by G. Wayne Choate, attached as Exhibit 1, and attached documents.

STATEMENT OF FACTS

Petitioner's showings are summarized in the following Statement of Facts:

Proof of Unavailability or Refusal:

1. Mr. Chaote declared under oath that he has first hand knowledge that complete copies of the application papers have been sent to the last known addresses of the nonsigning inventors and to what he understood to be their counsel. (Ex. 1, p. 9).

2. On May 1, 2001, he personally mailed to each inventor (Dr. Bachynsky and Ms. Roy), by U.S. Certified Mail, Return Receipt Requested, a separate letter enclosing a copy of the declaration to be signed for this patent application. The letter requested each inventor to execute the declarations in accordance with the assignment executed by such inventor, wherein each agreed to execute all declarations or other papers that are deemed necessary by Texas Pharmaceuticals, Inc. for filing and prosecuting patent applications (Assignments in Exhibits A1 and B1 to Exhibit 1). The letters were sent to the last known address of the inventors, being the same address to which a letter was sent on April 23, 2001, to Woodie E. Roy as a shareholder in Texas Pharmaceuticals, Inc. and was accepted by signature of Nicholas Bachynsky. That letter of April 23, 2001, confirmed that "future mailings ... will be furnished to you at the address

above shown until notice of change of address is furnished to the Corporation in accordance with the bylaws of the Corporation." Copies of these letters, including the return receipts reflecting delivery and receipt of each letter, are attached at Exhibit C to Exhibit 1. Mr. Choate's letter of May 1, 2001, provides that "[I]f the signed Declaration for Patent Assignment is not received in my office on or before May 14, 2001, I will assume that you have declined to execute this document." Mr. Choate received nothing in return except the return receipt for each letter and was not contacted by either Woodie E. Roy or Nicholas Bachynsky. (Ex. 1, pp. 9-10).

3. Mr. Choate did not anticipate that either inventor would provide any cooperation or would sign the Declaration for Patent Assignment because Texas Pharmaceuticals, Inc., acting through its President, had previously filed eviction proceedings against the inventors and had successfully evicted them from a dwelling owned by the President. (Ex. 1, p. 10).

4. Thereafter, on August 30, 2001, Mr. Choate received a letter from Harris K. Solomon, as attorney for Nicholas Bachynsky and Woodie Roy, which threatened litigation unless Texas Pharmaceuticals, Inc. voluntarily re-conveyed the subject matter of the assignments to the inventors. On April 29, 2002, Mr. Choate personally sent a letter by certified mail, return receipt requested, to Harris K. Solomon, as attorney for Nicholas Bachynsky and Woodie Roy, with copies of that letter sent to Nicholas Bachynsky and to Woodie Roy, by certified mail, return receipt requested. Complete copies of the present patent application (specification, claims, drawings and declaration), a copy of the declaration to be signed, and a cover letter explaining same were enclosed with this letter, with a renewed request for execution of the Declaration for Patent Assignment. A copy of this letter is attached as Exhibit D to Exhibit 1. These materials were also sent to all addresses by overnight courier. Mr. Choate received nothing in return other than the return receipts, acknowledging receipt of the letters by each recipient. Delivery by the overnight courier has been confirmed also (copies of which are attached at Exhibit D of Exhibit 1). (Ex. 1, pp. 10-11).

5. On May 6, 2002, Mr. Choate was contacted by telephone by Kevin P. Crosby and John Lambros of Mr. Solomon's firm, Brinkley, McNerney, Morgan, Solomon & Tatum, LLP, as counsel for the inventors. Mr. Crosby acknowledged actual receipt of the documents which Mr. Choate had mailed to Mr. Solomon and to Nicholas Bachynsky and Woodie Roy on April 29, 2002. (Ex. 1, p. 11).

6. Mr. Choate has first hand knowledge, and information and belief, that both inventors refused to sign a declaration for the above-referenced patent application. This is based in part upon his first hand knowledge of the following:

- **Mr. Choate sent the above-described materials to the inventors on May 1, 2001 and again on April 29, 2002, and received no response to same other than confirmation of receipt of delivery of the letters by certified mail, return receipt requested.** His letter of May 1, 2001, which was received by the inventors, clearly stated that the failure of the inventors to sign and return the enclosed Declarations for Patent Application on or before May 14, 2001, would be relied upon by Texas Pharmaceuticals, Inc. as the inventors' refusal to sign the submitted Declarations for Patent Application.

- **Mr. Choate's telephone conversation with Harris K. Solomon on September 11, 2001.** On that date, Mr. Choate spoke by telephone with Harris K. Solomon and was informed that neither Nicholas Bachynsky nor Woodie Roy would cooperate with Texas Pharmaceuticals, Inc. by signing the Declaration for Patent Assignment. Mr. Solomon stated the reason for this refusal was the inventors' belief and understanding that Texas Pharmaceuticals, Inc. had engaged in improper or illegal conduct with regard to the use and testing of the invention and that such alleged actions had or would destroy the future financial viability of the invention, to the detriment of Woodie Roy, who is a shareholder in Texas Pharmaceuticals, Inc.

- **Mr. Choate's telephone conversation on May 6, 2002, with Kevin P. Crosby and John Lambros, each as legal counsel for both inventors, who indicated that the inventors' refusal to sign the Declarations for Patent Assignment would impede Texas Pharmaceuticals, Inc.'s patent application and asserted their client's claim for re-assignment of rights in the invention.**

- **Mr. Choate's first hand knowledge, and information and belief, that both inventors were and are currently in a dispute with assignee.**

(Ex. 1, pp. 11-12).

Proof of Proprietary Interest:

The following written, documentary evidence is being submitted with this Renewed Petition which shows that the assignee, Texas Pharmaceuticals, Inc., has full proprietary interest in the invention. Mr. Choate has first hand knowledge of the preparation and execution of all of the attached documents, which show that the invention of the above-referenced application has been assigned by inventors to Texas Pharmaceuticals, Inc. and that it otherwise has full proprietary interest in the invention of the above-referenced application.

1. **Exhibit A: Agreement for Sale of Invention and Related Rights – Bachynsky**

Attached as Exhibit A to Exhibit 1 is an Agreement for Sale of Invention and Related Rights (by inventor Bachynsky) ("Agreement"), wherein inventor Nicholas Bachynsky sold all right, title and interest in the invention of the above-referenced patent application to assignee, Texas Pharmaceuticals, Inc. This agreement, dated March 2, 1998, was executed by inventor Nicholas Bachynsky on March 5, 1998, and by James J. Naples, on behalf of assignee, on March 6, 1998. This agreement was executed over one year prior to the filing of the above-referenced patent application and therefore could not include a reference to the patent application or identify the above-referenced patent application by application number. (Ex. 1, p. 3).

This document covers, in writing, the sale of rights to the invention as disclosed and claimed in the above-referenced patent application. This is shown, for example, in the Agreement which describes the sold invention as follows:

> Seller [Inventor Nicholas Bachynsky], with the financial support of James J. Naples, has been conducting medical research and developing a novel use and method of inducing intracellular hyperthermia and free radical flux through use of dinitrophenol and other mitochondrial uncoupling agents in the treatment of infectious and malignant disease. Seller has developed and devised a therapeutic application of dinitrophenol and other mitochondrial uncoupling agents for such purposes.

(Agreement, page 1, (Exhibit A)) (Ex. 1, pp. 3-4).

This is the same invention as the above-referenced patent application. This can be seen, for example, from the abstract of the instant application, which defines the invention as follows:

> An invention relating to therapeutic pharmacological agents and methods to chemically induce intracellular hyperthermia and/or free radicals for the diagnosis

> and treatment of infections, malignancy and other medical conditions. The invention relates to a process and composition for the diagnosis or killing of cancer cells and inactivation of susceptible bacteria, parasitic, fungal and viral pathogens by chemically generating heat, and/or free radicals or hyperthermia-inducible immunogenic determinants by using mitochondrial uncoupling agents, especially 2,4 dinitrophenol [dinitrophenol] either alone or in combination with other drugs, hormones, cytokines and radiation.

(Abstract, U.S. Application Serial No. 09/744,622) (Ex. 1, pp. 4).

The invention sold in the Agreement is also defined in Schedule 1 to Exhibit A of the Agreement (attached hereto as Exhibit A1), wherein it is defined as follows:

> This invention provides a medical treatment for ... treatment of resistant neoplastic and infectious disease by concurrent administration of dinitrophenol [or other mitochondrial thermoregulatory uncoupling agents ...] ... and specific metabolic, activating cytokines ... hormones... and other medications to control and focally enhance the mitochondrial uncoupling effects. ... A new use(s)/method of generating intracellular oxygen derived from free radicals, and heating from within the cell [intracellular hyperthermia] has been discovered for dinitrophenol (or other oxidative phosphorylation uncouplers) in prevention of parasites .. bacteria ... viruses... and neoplasia..."

(Ex. 1, p. 4).

This description of the invention as sold in the Agreement directly matches the invention described in the present application, as can be seen, for example, from the abstract of the application, quoted above. (Ex. 1, p. 5).

Moreover, the working example defining the invention sold in the Agreement, as defined in Schedule 1 to Exhibit A of the Agreement (attached at Exhibit A1), is identical to Example 1 of the above-referenced application (see pages 38 – 40 and Table 15). (Ex. 1, p. 5).

Further still, the description of the invention sold in the agreement, as defined in Schedule 1 to Exhibit A of the Agreement (attached at Exhibit A1, discussed above), is identical to the description of the invention in the attachments to the Assignment of inventor Nicholas Bachynsky, as filed in this case (Exhibit A1 (recorded in this case with the U.S. Patent and Trademark Office at Reel/Frame 012063/0015)). (Ex. 1, p. 5).

Further in support, the Agreement is accompanied by an executed Assignment of rights by Dr. Bachynsky to assignee (Exhibit A1, discussed below), a Non-Competition Agreement

executed by Dr. Bachynsky (Exhibit A2), a promissory note to Nicholas Bachynsky, executed by assignee (Exhibit A3), and a Security Agreement between assignee and Dr. Bachynsky (Exhibit A4), a Warrant of Assignee, executed by assignee (Exhibit A5), and an Attorney Representation Statement executed by Dr. Bachynsky (Exhibit A6). (Ex. 1, p. 5).

2. **Exhibit A1: Assignment by inventor Nicholas Bachynsky**

Exhibit A1 to Exhibit 1 is a copy of an Assignment by inventor Nicholas Bachynsky assigning to assignee, Texas Pharmaceuticals, Inc., all right, title and interest in the invention of the present application. As discussed above, the definition of the invention in this assignment is identical to the invention sold by Dr. Bachynsky to assignee and is identical to the invention of the instant application. The assignment was executed on March 4, 1998, many months prior to the filing of the above-referenced patent application on July 27, 1999, and therefore, the assignment could not refer to or identify the application number for the above-referenced patent application, as it did not exist on March 4, 1998. (Ex. 1, pp. 5-6).

3. **Exhibit B: Agreement for Sale of Invention and Related Rights -- Roy**

Attached as Exhibit B to Exhibit 1 is an Agreement for Sale of Invention and Related Rights (by inventor Roy) ("Agreement#2"), wherein inventor Woodie Roy sold all right, title and interest in the invention of the above-referenced patent application to assignee, Texas Pharmaceuticals, Inc. This agreement, dated July 20, 1998, was executed by inventor Woodie Roy on July 24, 1998, and by James J. Naples, on behalf of assignee, on July 24, 1998. This agreement was executed well in advance of the filing of the above-referenced patent application on July 27, 1999, and therefore could not include a reference to or identify the application number for the above-referenced patent application. (Ex. 1, p. 6).

This document covers, in writing, the sale of rights to the invention as disclosed and claimed in the above-referenced patent application. This is shown, for example, in the Agreement which describes the sold invention as follows:

> Seller has assisted [inventor] Nicolas Bachynsky ("Bachynsky") who, with the financial support of James J. Naples, has been conducting medical research and developing a novel use and method of inducing intracellular hyperthermia and free radical flux through use of dinitrophenol and other mitochondrial uncoupling agents in the treatment of infectious and malignant disease. Bachynsky and seller

> have developed and devised a therapeutic application of dinitrophenol and other mitochondrial uncoupling agents for such purposes.

(Agreement, page 1, (Exhibit B)) (Ex. 1, pp. 6-7).

This is the same invention as the above-referenced patent application, which can be seen by reference to the application's abstract (quoted above). (Ex. 1, p. 7).

The invention sold in the Agreement#2 is also defined in Schedule 1 to Exhibit A of the Agreement#2 (attached hereto as Exhibit B1), wherein it is defined as follows:

> This invention provides a medical treatment for ... treatment of resistant neoplastic and infectious disease by concurrent administration of dinitrophenol [or other mitochondrial thermoregulatory uncoupling agents ...] ... and specific metabolic, activating cytokines ... hormones... and other medications to control and focally enhance the mitochondrial uncoupling effects. ... A new use(s)/method of generating intracellular oxygen derived from free radicals, and heating from within the cell [intracellular hyperthermia] has been discovered for dinitrophenol (or other oxidative phosphorylation uncouplers) in prevention of parasites .. bacteria ... viruses... and neoplasia..."

(Ex. 1, p. 7).

This description of the invention as sold in the Agreement directly matches the invention described in the present application, as can be seen, for example, from the abstract of the application, discussed above. (Ex. 1, p. 7).

Moreover, the working example defining the invention sold in the Agreement#2, as defined in Schedule 1 to Exhibit A of the Agreement#2 (attached at Exhibit B1), is identical to Example 1 of the above-referenced application (see pages 38 – 40 and Table 15). (Ex. 1, p. 7).

Further still, the description of the invention sold in the Agreement#2, as defined in Schedule 1 to Exhibit A of the Agreement#2 (attached at Exhibit B1, discussed above), is identical to the description of the invention of the present invention as found in the attachments to the Assignment of inventor Woodie Roy, as filed in this case (see Exhibit B1, recorded in this case with the U.S. Patent and Trademark Office at Reel/Frame 012063/0023). (Ex. 1, p. 8).

Further in support, Agreement#2 is accompanied by an executed Assignment of rights by inventor Woodie Roy to assignee (Exhibit B1, discussed below), a Non-Competition Agreement executed by Ms. Roy (Exhibit B2), a Warrant of Assignee, executed by assignee (Exhibit B3), and an Affidavit As To Fact (Exhibit B4, discussed below). (Ex. 1, p. 8).

4. **Exhibit B1: Assignment by inventor Woodie Roy**

Exhibit B1 to Exhibit 1 is a copy of an Assignment by inventor Woodie Roy assigning to assignee, Texas Pharmaceuticals, Inc., all rights and title to the invention of the present application (as discussed above). As discussed above, the definition of the invention in this assignment is identical to the invention sold by Ms. Roy to assignee and is identical to the invention of the instant application. This assignment was executed well in advance of the filing of the above-referenced patent application on July 27, 1999, and therefore, this assignment could not include a reference to or identify the application number for the above-referenced patent application. (Ex. 1, p. 8).

5. **Exhibit B4: Affidavit As To Fact by inventor Woodie Roy**

Exhibit B4 to Exhibit 1 is an Affidavit As To Fact by inventor Woodie Roy wherein she reiterates that she assigned all interest, right and title in the invention of the present patent application to the assignee, Texas Pharmaceuticals, Inc. For example, Ms. Roy states:

> I recognize and confirm that Texas Pharmaceuticals, Inc. and/or James J. Naples have expended money to research the viability of this application of dinitrophenol and have done so with the understanding that Texas Pharmaceuticals, Inc. would own the commercial rights to any patent or therapy involving the use of dinitrophenol in the treatment of malignant and infectious diseases.
>
> As set forth in my Assignment of my rights to Texas Pharmaceuticals, Inc., I have conveyed all of my right, title and interest in the use of dinitrophenol as therein described for the sole purpose of vesting in Texas Pharmaceuticals, Inc. such rights.

(Affidavit As To Fact, page 1, Exhibit B4) (Ex. 1, p. 9).

Additional Relevant Facts:

1. **The inventors signed a declaration for the provisional application.** Mr. Choate has first hand knowledge that both inventors signed a declaration for the provisional patent application which discloses the invention, and is claimed as a priority document in the above-referenced application. A copy of these signed declarations are attached as Exhibit E to Exhibit 1. This application was also assigned to assignee, as shown in the Assignments attached in Exhibit E (recorded with the U.S. Patent and Trademark Office at Reel/Frame 010993/0076 (Bachynsky) and 010992/0945 (Roy)).

2. **James J. Naples is the President of assignee and has full authority to execute the declaration on behalf of the assignee.** Mr. Choate has first hand information and belief that James J. Naples is the President of Texas Pharmaceuticals, Inc. and has full authority to execute the declaration on behalf of the assignee.

3. **Filing the above-referenced patent application under 37 C.F.R. § 1.47(b) is necessary to preserve the rights of the rights of the parties and to prevent irreparable damage which otherwise would result with the application becoming abandoned.** Mr. Choate has first hand information and belief that filing the above-referenced patent application with James Naples signing the declaration for assignee in lieu of the inventors (filing the application under 37 C.F.R. § 1.47(b)) is necessary in order to preserve the rights of the rights of the parties and to prevent irreparable damage which otherwise would result with the application becoming abandoned.

4. **Filing the above-referenced patent application under 37 C.F.R. § 1.47(b) is necessary to preserve the rights of the rights of the parties and to prevent irreparable damage which otherwise would result with the application becoming abandoned.** Mr. Choate declared upon information and belief that filing the above-referenced patent application with James Naples signing the declaration for assignee in lieu of the inventors (filing the application under 37 C.F.R. § 1.47(b)) is necessary in order to preserve the rights of the rights of the parties and to prevent irreparable damage which otherwise would result with the application becoming abandoned.

CONCLUSION

For the reasons stated above, and as supported by the attachments hereto, assignee respectfully asserts that the above-referenced application is proper for, and should be accepted with, a declaration under 37 C.F.R. § 1.47(b).

The last known addresses of the inventors, and their attorney, are:

Nicholas Bachynsky
6090 N.W. 66th Street
Parkland, Florida 33067

Woodie Roy
6090 N.W. 66th Street
Parkland, Florida 33067

Harris K. Solomon
Brinkley, McNerney, Morgan, Soloman & Tatum, L.L.P.
200 East Las Olas Boulevard
Suite 1900
Fort Lauderdale, Florida 33301-2209

Please charge the deposit account of Fulbright & Jaworski LLP, Account No. 06-2375, under order no. 09805783 for any fees that may be necessary.

Respectfully submitted,

Paul E. Krieger
Registration No.: 25,886

Date: November 27, 2002
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Nicholas Bachynsky Woodie Roy	§	
	§	Group Art Unit: Unknown
Serial No.: 09/744622 (PCT/US99/16940)	§	
	§	Examiner: Unassigned
Filed: January 26, 2001	§	
	§	Atty. Docket: P01615US1 / 09805783
For: **CHEMICALLY INDUCED INTRACELLULAR HYPERTHERMIA**	§	(U.S. Nat'l. Phase)

SUPPLEMENTAL DECLARATION

IN SUPPORT OF RENEWED PETITION UNDER 37 C.F.R. 1.47(B)

I, G. Wayne Choate, am an attorney at law in the State of Texas, and am a shareholder in the law firm of Goode, Casseb, Jones, Riklin, Choate & Watson, a Professional Corporation organized under the laws of the State of Texas, located at 2122 North Main Avenue, San Antonio, Texas 78212 ("the Firm"). The Firm represents Texas Pharmaceuticals, Inc., a Texas corporation, located at 701 West 14th Street, Texarkana, Texas 75501 ("assignee").

I have first hand knowledge of the following facts, and attached supporting documentation, which show that:

- i) assignee has full proprietary interest in the above-referenced patent application, application number 09/744,622 (PCT/US99/16940), and the subject matter of such patent application ("the invention"), specifically, the invention and all related rights

have been assigned to assignee by written assignments executed by the inventors, Nicholas Bachynsky and Woodie Roy, ("inventors");

- ii) a copy of the application papers for the invention have been sent to the last known address of the inventors and to the attention of the person believed to be the attorney for the inventors requesting execution of the application papers in accordance with the agreements executed by the inventors;

- iii) despite providing such application papers by certified mail, return receipt requested on two occasions, the inventors failed to respond to requests for execution of the application papers and the inventors' attorney stated that his clients would not execute the application papers;

- iv) the inventors signed a declaration in the provisional patent application claimed as a priority document to this application;

- v) James J. Naples is the President of assignee and has full authority to execute the declaration on behalf of assignee; and

- vi) filing the above-referenced patent application under 37 C.F.R. § 1.47(b) is necessary to preserve the rights of the rights of the parties and to prevent irreparable damage which otherwise would result with the application becoming abandoned.

The assignee has proprietary interest in the invention

The following written, documentary evidence is being submitted herewith showing that the assignee has full proprietary interest in the invention. I have first hand knowledge of the preparation and execution of all of the attached documents, which show that the invention of the above-referenced application has been assigned by inventors to assignee and that assignee otherwise has full proprietary interest in the invention of the above-referenced application.

Exhibit A: Agreement for Sale of Invention and Related Rights – Bachynsky

Attached as Exhibit A is an Agreement for Sale of Invention and Related Rights (by inventor Bachynsky) ("Agreement"), wherein inventor Nicholas Bachynsky sold all right, title and interest in the invention of the above-referenced patent application to assignee, Texas Pharmaceuticals, Inc. This agreement, dated March 2, 1998, was executed by inventor Nicholas Bachynsky on March 5, 1998, and by James J. Naples, on behalf of assignee, on March 6, 1998. This agreement was executed over one year prior to the filing of the above-referenced patent application and therefore could not include a reference to the patent application or identify the above-referenced patent application by application number.

This document covers, in writing, the sale of rights to the invention as disclosed and claimed in the above-referenced patent application. This is shown, for example, in the Agreement which describes the sold invention as follows:

> Seller [Inventor Nicholas Bachynsky], with the financial support of James J. Naples, has been conducting medical research and

> developing a novel use and method of inducing intracellular hyperthermia and free radical flux through use of dinitrophenol and other mitochondrial uncoupling agents in the treatment of infectious and malignant disease. Seller has developed and devised a therapeutic application of dinitrophenol and other mitochondrial uncoupling agents for such purposes.
>
> (Agreement, page 1, (Exhibit A)).

This is the same invention as the above-referenced patent application. This can be seen, for example, from the abstract of the instant application, which defines the invention as follows:

> An invention relating to therapeutic pharmacological agents and methods to chemically induce intracellular hyperthermia and/or free radicals for the diagnosis and treatment of infections, malignancy and other medical conditions. The invention relates to a process and composition for the diagnosis or killing of cancer cells and inactivation of susceptible bacteria, parasitic, fungal and viral pathogens by chemically generating heat, and/or free radicals or hyperthermia-inducible immunogenic determinants by using mitochondrial uncoupling agents, especially 2,4 dinitrophenol [dinitrophenol] either alone or in combination with other drugs, hormones, cytokines and radiation.
>
> (Abstract, U.S. Application Serial No. 09/744,622).

The invention sold in the Agreement is also defined in Schedule 1 to Exhibit A of the Agreement (attached hereto as Exhibit A1), wherein it is defined as follows:

> This invention provides a medical treatment for ... treatment of resistant neoplastic and infectious disease by concurrent administration of dinitrophenol [or other mitochondrial thermoregulatory uncoupling agents ...] ... and specific metabolic, activating cytokines ... hormones... and other medications to control and focally enhance the mitochondrial uncoupling effects. ... A new use(s)/method of generating intracellular oxygen derived from free radicals, and heating from within the cell [intracellular hyperthermia] has been discovered for dinitrophenol (or other oxidative phosphorylation uncouplers) in prevention of parasites .. bacteria ... viruses... and neoplasia..."

This description of the invention as sold in the Agreement directly matches the invention described in the present application, as can be seen, for example, from the abstract of the application, quoted above.

Moreover, the working example defining the invention sold in the Agreement, as defined in Schedule 1 to Exhibit A of the Agreement (attached at Exhibit A1), is identical to Example 1 of the above-referenced application (see pages 38 – 40 and Table 15).

Further still, the description of the invention sold in the agreement, as defined in Schedule 1 to Exhibit A of the Agreement (attached at Exhibit A1, discussed above), is identical to the description of the invention in the attachments to the Assignment of inventor Nicholas Bachynsky, as filed in this case (Exhibit A1 (recorded in this case with the U.S. Patent and Trademark Office at Reel/Frame 012063/0015)).

Further in support, the Agreement is accompanied by an executed assignment of rights by Dr. Bachynsky to assignee (Exhibit A1, discussed below), a Non-Competition Agreement executed by Dr. Bachynsky (Exhibit A2), a promissory note to Nicholas Bachynsky, executed by assignee (Exhibit A3), and a Security Agreement between assignee and Dr. Bachynsky (Exhibit A4), a Warrant of Assignee, executed by assignee (Exhibit A5), and an Attorney Representation Statement executed by Dr. Bachynsky (Exhibit A6).

Exhibit A1: Assignment by inventor Nicholas Bachynsky

Exhibit A1 is a copy of an assignment by inventor Nicholas Bachynsky assigning to assignee, Texas Pharmaceuticals, Inc., all right, title and interest in the invention of the

present application. As discussed above, the definition of the invention in this assignment is identical to the invention sold by Dr. Bachynsky to assignee and is identical to the invention of the instant application. The assignment was executed on March 4, 1998, many months prior to the filing of the above-referenced patent application on July 27, 1999, and therefore, the assignment could not refer to or identify the application number for the above-referenced patent application, as it did not exist on March 4, 1998.

Exhibit B: Agreement for Sale of Invention and Related Rights -- Roy

Attached as Exhibit B is an Agreement for Sale of Invention and Related Rights (by inventor Roy) ("Agreement#2"), wherein inventor Woodie Roy sold all right, title and interest in the invention of the above-referenced patent application to assignee, Texas Pharmaceuticals, Inc. This agreement, dated July 20, 1998, was executed by inventor Woodie Roy on July 24, 1998, and by James J. Naples, on behalf of assignee, on July 24, 1998. This agreement was executed well in advance of the filing of the above-referenced patent application on July 27, 1999, and therefore could not include a reference to or identify the application number for the above-referenced patent application.

This document covers, in writing, the sale of rights to the invention as disclosed and claimed in the above-referenced patent application. This is shown, for example, in the Agreement which describes the sold invention as follows:

> Seller has assisted [inventor] Nicolas Bachynsky ("Bachynsky") who, with the financial support of James J. Naples, has been conducting medical research and developing a novel use and method of inducing intracellular hyperthermia and free radical flux through use of dinitrophenol and other mitochondrial uncoupling

> agents in the treatment of infectious and malignant disease. Bachynsky and seller have developed and devised a therapeutic application of dinitrophenol and other mitochondrial uncoupling agents for such purposes.
>
> (Agreement, page 1, (Exhibit B)).

This is the same invention as the above-referenced patent application, which can be seen by reference to the application's abstract (quoted above).

The invention sold in the Agreement#2 is also defined in Schedule 1 to Exhibit A of the Agreement#2 (attached hereto as Exhibit B1), wherein it is defined as follows:

> This invention provides a medical treatment for ... treatment of resistant neoplastic and infectious disease by concurrent administration of dinitrophenol [or other mitochondrial thermoregulatory uncoupling agents ...] ... and specific metabolic, activating cytokines ... hormones... and other medications to control and focally enhance the mitochondrial uncoupling effects. ... A new use(s)/method of generating intracellular oxygen derived from free radicals, and heating from within the cell [intracellular hyperthermia] has been discovered for dinitrophenol (or other oxidative phosphorylation uncouplers) in prevention of parasites .. bacteria ... viruses... and neoplasia..."

This description of the invention as sold in the Agreement directly matches the invention described in the present application, as can be seen, for example, from the abstract of the application, discussed above.

Moreover, the working example defining the invention sold in the Agreement#2, as defined in Schedule 1 to Exhibit A of the Agreement#2 (attached at Exhibit B1), is identical to Example 1 of the above-referenced application (see pages 38 – 40 and Table 15).

Further still, the description of the invention sold in the Agreement#2, as defined in Schedule 1 to Exhibit A of the Agreement#2 (attached at Exhibit B1, discussed above), is identical to the description of the invention of the present invention as found in the attachments to the assignment of inventor Woodie Roy, as filed in this case (see Exhibit B1, recorded in this case with the U.S. Patent and Trademark Office at Reel/Frame 012063/0023).

Further in support, Agreement#2 is accompanied by an executed assignment of rights by inventor Woodie Roy to assignee (Exhibit B1, discussed below), a Non-Competition Agreement executed by Ms. Roy (Exhibit B2), a Warrant of Assignee, executed by assignee (Exhibit B3), and an Affidavit As To Fact (Exhibit B4, discussed below).

Exhibit B1: Assignment by inventor Woodie Roy

Exhibit B1 is a copy of an assignment by inventor Woodie Roy assigning to assignee, Texas Pharmaceuticals, Inc., all rights and title to the invention of the present application (as discussed above). As discussed above, the definition of the invention in this assignment is identical to the invention sold by Ms. Roy to assignee and is identical to the invention of the instant application. This assignment was executed well in advance of the filing of the above-referenced patent application on July 27, 1999, and therefore, this assignment could not include a reference to or identify the application number for the above-referenced patent application.

Exhibit B4: Affidavit As To Fact by inventor Woodie Roy

Exhibit B4 is an Affidavit As To Fact by inventor Woodie Roy wherein she reiterates that she assigned all interest, right and title in the invention of the present patent application to the assignee, Texas Pharmaceuticals, Inc. For example, Ms. Roy states:

> I recognize and confirm that Texas Pharmaceuticals, Inc. and/or James J. Naples have expended money to research the viability of this application of dinitrophenol and have done so with the understanding that Texas Pharmaceuticals, Inc. would own the commercial rights to any patent or therapy involving the use of dinitrophenol in the treatment of malignant and infectious diseases.
>
> As set forth in my Assignment of my rights to Texas Pharmaceuticals, Inc., I have conveyed all of my right, title and interest in the use of dinitrophenol as therein described for the sole purpose of vesting in Texas Pharmaceuticals, Inc. such rights.
>
> (Affidavit As To Fact, page 1, Exhibit B4).

Complete copies of the application papers have been sent to the last known addresses of the nonsigning inventors and to what is understood to be their counsel

I have first hand knowledge of the fact that complete copies of the application papers have been sent to the last known addresses of the nonsigning inventors and to what is understood to be their counsel.

Specifically, on May 1, 2001, I personally mailed to each inventor (Dr. Bachynsky and Ms. Roy), by U.S. Certified Mail, Return Receipt Requested, a separate letter enclosing a copy of the declaration to be signed for this patent application. The letter requested each inventor to execute the declarations in accordance with the

assignment executed by such inventor, wherein each agreed to execute all declarations or other papers that are deemed necessary by Texas Pharmaceuticals, Inc. for filing and prosecuting patent applications (assignments in Exhibits A1 and B1). The letters were sent to the last known address of the inventors, being the same address to which a letter was sent on April 23, 2001, to Woodie E. Roy as a shareholder in Texas Pharmaceuticals, Inc. and was accepted by signature of Nicholas Bachynsky. That letter of April 23, 2001, confirmed that "future mailings ... will be furnished to you at the address above shown until notice of change of address is furnished to the Corporation in accordance with the bylaws of the Corporation." Copies of these letters, including the return receipts reflecting delivery and receipt of each letter, are attached at Exhibit C. The letter of May 1, 2001, provides that "[I]f the signed Declaration for Patent Assignment is not received in my office on or before May 14, 2001, I will assume that you have declined to execute this document." I received nothing in return except the return receipt for each letter and was not contacted by either Woodie E. Roy or Nicholas Bachynsky.

I did not anticipate that either inventor would provide any cooperation or would sign the Declaration for Patent Assignment because Texas Pharmaceuticals, Inc., acting through its President, have previously filed eviction proceedings against the inventors and had successfully evicted them from a dwelling owned by the President.

Thereafter, on August 30, 2001, I received a letter from Harris K. Solomon, as attorney for Nicholas Bachynsky and Woodie Roy, which threatened litigation unless Texas Pharmaceuticals, Inc. voluntarily re-conveyed the subject matter of the assignments to the inventors. On April 29, 2002, I personally sent a letter by certified mail, return receipt requested to Harris K. Solomon, as attorney for Nicholas Bachynsky

and Woodie Roy, with copies of that letter sent to Nicholas Bachynsky and to Woodie Roy, by certified mail, return receipt requested. Complete copies of the present patent application (specification, claims, drawings and declaration), a copy of the declaration to be signed, and a cover letter explaining same were enclosed with this letter, with a renewed request for execution of the Declaration for Patent Assignment. A copy of this letter is attached as Exhibit D. These materials were also sent to all addresses by overnight courier. I received nothing in return other than the return receipts, acknowledging receipt of the letters by each recipient. Delivery by the overnight courier has been confirmed also (copies of which are attached at Exhibit D).

On May 6, 2002, I was contacted by telephone by Kevin P. Crosby and John Lambros of Mr. Solomon's firm, Brinkley, McNerney, Morgan, Solomon & Tatum, LLP, as counsel for the inventors. Mr. Crosby acknowledged actual receipt of the documents which I had mailed to Mr. Solomon and to Nicholas Bachynsky and Woodie Roy on April 29, 2002.

The inventors refuse to sign the declarations

I have first hand knowledge, and information and belief, that both inventors refuse to sign a declaration for the above-referenced patent application. This is based in part upon my first hand knowledge of the following

- My sending the above-described materials to the inventors on May 1, 2001 and again on April 29, 2002, and receiving no response to same other than confirmation of receipt of delivery of the letters by certified mail, return receipt requested. My letter of May 1, 2001, which was received by the

inventors, clearly stated that the failure of the inventors to sign and return the enclosed Declarations for Patent Application on or before May 14, 2001, would be relied upon by Texas Pharmaceuticals, Inc. as the inventors' refusal to sign the submitted Declarations for Patent Application.

- My telephone conversation with Harris K. Solomon on September 11, 2001. On that date, I spoke by telephone with Harris K. Solomon and was informed that neither Nicholas Bachynsky nor Woodie Roy would cooperate with Texas Pharmaceuticals, Inc. by signing the Declaration for Patent Assignment. Mr. Solomon stated the reason for this refusal was the inventors' belief and understanding that Texas Pharmaceuticals, Inc. had engaged in improper or illegal conduct with regard to the use and testing of the invention and that such alleged actions had or would destroy the future financial viability of the invention, to the detriment of Woodie Roy, who is a shareholder in Texas Pharmaceuticals, Inc.

- My telephone conversation on May 6, 2002, with Kevin P. Crosby and John Lambros, each as legal counsel for both inventors, who indicated that the inventors' refusal to sign the Declarations for Patent Assignment would impede Texas Pharmaceuticals, Inc.'s patent application and asserting their client's claim for re-assignment of rights in the invention.

- My first hand knowledge, and information and belief, that both inventors were and are currently in a dispute with Texas Pharmaceuticals, Inc.

The inventors signed a declaration for the provisional application

I have first hand knowledge that both inventors signed a declaration for the provisional patent application which discloses the invention, and is claimed as a priority document in the above-referenced application. A copy of these signed declarations are attached as Exhibit E. This application was also assigned to assignee, as shown in the assignments attached in Exhibit E (recorded with the U.S. Patent and Trademark Office at Reel/Frame 010993/0076 (Bachynsky) and 010992/0945 (Roy)).

James J. Naples is the President of assignee and has full authority to execute the declaration on behalf of the assignee

I have first hand information and belief that James J. Naples is the President of Texas Pharmaceuticals, Inc. and has full authority to execute the declaration on behalf of the assignee.

Filing the above-referenced patent application under 37 C.F.R. § 1.47(b) is necessary to preserve the rights of the rights of the parties and to prevent irreparable damage which otherwise would result with the application becoming abandoned

I have first hand information and belief that filing the above-referenced patent application with James Naples signing the declaration for assignee in lieu of the inventors (filing the application under 37 C.F.R. § 1.47(b)) is necessary in order to preserve the rights of the rights of the parties and to prevent irreparable damage which otherwise would result with the application becoming abandoned.

The undersigned being hereby warned that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001, and that such willful false statements and the like may jeopardize the validity of the application or any patent issuing therefrom, I declare that all statements made herein by my own knowledge are true, and that all statements made herein on information and belief are believed to be true.

G. Wayne Choate

Date: November 6 2002

AGREEMENT FOR SALE OF INVENTION AND RELATED RIGHTS

THIS AGREEMENT FOR SALE OF INVENTION AND RELATED RIGHTS (this "Agreement") is made and entered into as of March 2, 1998, by and among, NICHOLAS BACHYNSKY, whose address for the purposes of this Agreement is c/o 701 W. 14th Street, Texarkana, Bowie County, Texas 75501 (herein, "Seller"), and TEXAS PHARMACEUTICALS, INC., a Texas corporation, whose address for the purposes of this Agreement is 701 W. 14th Street, Texarkana, Bowie County, Texas 75501 (herein "Purchaser").

F A C T S

Seller, with the financial support of James J. Naples, has been conducting medical research and developing a novel use and method of inducing intracellular hyperthermia and free radical flux through the use of dinitrophenol and other mitochondrial uncoupling agents in the treatment of infectious and malignant disease. Seller has developed and devised a therapeutic application of dinitrophenol and other mitochondrial uncoupling agents for such purposes. A description of this therapy is attached as Schedule 1 to Exhibit A to this Agreement and the matters described therein and herein are referred to herein, collectively, as the "Invention".

Seller desires to sell Seller's entire right, title and interest in and to such Invention and any and all patents and protections which may hereafter be obtained regarding the Invention (the "Patent Rights"), and Purchaser desires to purchase the Patent Rights, upon the terms and conditions hereinafter set forth.

NOW, THEREFORE, in consideration of the mutual benefits to be derived and the representations and warranties, conditions and promises herein contained, and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, and intending to be legally bound hereby, the parties agree as follows:

ARTICLE I

GENERAL

1.01 Definitions. Unless otherwise stated in this Agreement, the following terms shall have the indicated meanings (the following definitions to be equally applicable to both the singular and plural forms of any of the terms herein defined):

"Assets": The assets, rights, interests and properties which are described in Section 1.02 (a) of this Agreement.

"Assignment": The Assignment from Seller, as assignor, to Purchaser, as assignee, in the form attached hereto as Exhibit A.

"Closing": The consummation of the purchase and sale contemplated by this Agreement.

"Closing Date": Wednesday, March 4, 1998 at 1:00 P.M., San Antonio, Texas time, or such other date and time upon which the parties may agree.

"Invention": Seller's invention of a novel use and method of inducing intracellular hyperthermia and free radical flux through the use of dinitrophenol and other mitochondrial uncoupling agents in the treatment of infectious and malignant disease, as more fully set forth in Schedule 1 to the form of Assignment attached hereto as Exhibit A.

"Non-Competition Agreement": The Non-Competition Agreement by and between Seller and Purchaser in the form attached hereto as Exhibit B.

"Patent Rights": The Invention, all of Seller's rights thereunder and therein, all existing and future patent applications relating to the Invention, all patents issued with respect to the Invention, all patents to be issued with respect to the Invention, all renewals or extensions or continuations of patents or patent applications with respect to the Invention, all causes of action relating to any use of the Invention and all international rights of priority with respect to said Invention and all rights to file further applications for patent or patent-like protections for said Invention.

"Promissory Note": The Promissory Note in the amount of $35,000.00 payable to Seller by Purchaser, evidencing a portion of the Purchase Price, in the form attached hereto as Exhibit C.

"Purchase Price": The price to be paid by Purchaser to Seller in consideration for the sale by Seller and Purchase by Purchaser of the Assets.

"Records": All of Seller's books, records, papers and instruments of whatever nature and wherever located that relate to the Patent Rights or which are required or necessary in order for Purchaser to fully utilize the economic benefits of the Patent Rights and Invention.

"Security Agreement": The Security Agreement executed by Seller and Purchaser, giving and granting to Seller a lien on the Assets to secure the repayment of the Promissory Note, in the form attached hereto as Exhibit D.

"Transaction": The sale and purchase of the Assets, assignment and assumption of certain rights and interests, and performance of the covenants, in each case as contemplated by this Agreement.

1.02. Agreement To Purchase and Sell.

(a) On and subject to the terms and conditions of this Agreement, Seller agrees to sell, convey, transfer, assign and deliver to Purchaser, and Purchaser agrees to purchase from Seller, the Invention, Patent Rights and Records.

(b) Seller agrees to enter into and be bound by the Non-Competition Agreement.

(c) Seller agrees to indemnify and hold harmless Purchaser in accordance with the terms of this Agreement.

1.03. Purchase Price. The Purchase Price for the Assets will be the total cash sum of TWO HUNDRED THOUSAND AND NO/100 DOLLARS ($200,000.00).

1.04. Payment of Purchase Price. The Purchase Price shall be payable to Seller by Purchaser as follows:

(a) On or before the Closing Date, James J. Naples has paid in excess of the sum of $165,000.00 in research and testing fees to the Cancer, Research and Therapy Center in San Antonio, Texas, and to research laboratories in Syracuse, New York, to or for the benefit of Seller. It is understood and agreed that Purchaser is presently entitled to a credit against the cash consideration payable to Seller by virtue of these cash payments or obligations incurred by James J. Naples to or for the benefit of Seller prior to the date of this Agreement. Payments were made by James J. Naples prior to the date of this Agreement, and prior to the date of incorporation of Purchaser, in anticipation of this Agreement to fund the costs of research and development of the Invention.

(b) On the Closing Date, Purchaser shall execute and deliver to Seller the Promissory Note and the Security Agreement. It is further understood and agreed that Purchaser shall be entitled to a credit against such promissory note for additional sums advanced by James J. Naples to or for the benefit of Seller to fund additional costs of research and development of the Invention.

1.05 No Assumption of Liabilities. By purchase of the Assets, Purchaser takes the assets free of any claims, liens or interests of third parties, other than the liens created to secure the repayment of the Promissory Note.

1.06 No Proration of Taxes; Offset. If any taxes of any kind are assessed against any of the Assets, Seller will pay such sums to the appropriate taxing authorities when due, prior to becoming delinquent, shall indemnify Purchaser for all such sums and, in addition to the indemnities hereinafter made, does give and grant to Purchaser an offset against all sums owing and unpaid under the Promissory Note for any amounts owed by Seller which Seller fails to pay.

1.07 Instruments of Transfer; Further Assurances. In order to consummate the Transaction, on the Closing Date the Seller shall deliver to Purchaser an executed and acknowledged, where applicable, original of (a) the Assignment, covering all of the Assets; and (b) the Non-Competition Agreement. At the Closing, and at all times thereafter as may be necessary, Seller agrees to execute and deliver to Purchaser such other instruments or transfers as may be reasonably necessary to vest in Purchaser good and indefeasible title to the Assets and to comply with the purposes and intent of this Agreement.

ARTICLE II

REPRESENTATIONS AND WARRANTIES

2.01. Representations and Warranties of Seller. Seller hereby represents and warrants to Purchaser that the following matters are true and correct on the date of this Agreement and will be true and correct through the Closing Date and thereafter, as if made on and as of that date:

(a) This Agreement constitutes the legal, valid and binding obligation of Seller, enforceable in accordance with its terms; no person or entity other than Seller has any interest in or ownership of the Invention as of the date of this Agreement other than equitable claims of Purchaser and/or James J. Naples by virtue of sums advanced to fund the costs of research and development of the Invention.

(b) Seller has good and indefeasible title to the Assets, free and clear of all liens and claims of third parties and no third party has any right to acquire the Assets superior to Purchaser.

(c) There are no claims, actions, suits or proceedings pending or threatened against Seller which involve any of the Assets.

(d) Seller has complied in all respects with all applicable laws, ordinances, regulations, statutes, rules and restrictions relating to the Assets, or any part thereof.

(e) There is no fact known to Seller which has specific application to this Transaction or the Assets which could have a material adverse effect on the Assets, the ability of Purchaser obtaining a patent on the Invention, the title of Purchaser in and to the Assets from and after the Closing or any other matter which would adversely impact Purchaser in connection with the Assets.

(f) Seller may execute, deliver and perform this Agreement without the necessity of Seller obtaining any consent, approval, authorization or waiver or giving notice or otherwise, except for such consents, approvals, authorizations,

waivers and notices which have been obtained and are unconditional and such notices which have been given.

(g) Seller has not incurred any trade payables which have not been disclosed to Purchaser and shall pay or otherwise satisfy all other claims and liabilities relating to the Assets incurred through the Closing Date. **SELLER AGREES AND DOES HEREBY INDEMNIFY AND HOLD PURCHASER HARMLESS FROM AND AGAINST ALL CLAIMS, LOSSES, DEMANDS, DAMAGES, LIABILITIES, COSTS AND EXPENSES RESULTING FROM OR RELATING TO ANY CLAIM MADE AGAINST PURCHASER ARISING FROM SELLER'S BREACH OF THIS AGREEMENT OR ANY OF ITS TERMS, SUCH AGREEMENT TO SURVIVE THE CLOSING OR ANY TERMINATION OF THIS AGREEMENT.**

2.02 Representations and Warranties of Purchaser. Purchaser represents and warrants to Seller that the following are true and correct on the date of this Agreement and will be true and correct through the Closing Date, as if made on and as of that date:

(a) This Agreement constitutes the legal, valid and binding obligation of Purchaser, enforceable in accordance with its terms.

(b) Purchaser may execute, deliver and perform this Agreement without the necessity of Purchaser obtaining any consent, approval, authorization or waiver or giving notice or otherwise, except for such consents, approvals, authorizations, waivers and notices which have been obtained and are unconditional and such notices which have been given.

ARTICLE III

CONDITIONS OF CLOSING

3.01. Conditions Imposed by Purchaser. The obligations of Purchaser to consummate the purchase and sale under this Agreement are subject to the satisfaction of the following conditions, each of which may be waived in writing by Purchaser:

(a) Seller shall have delivered to Purchaser the duly executed and acknowledged Assignment.

(b) Seller shall have delivered to Purchaser the duly executed and acknowledged the Non-Competition Agreement.

(c) Seller shall have performed the covenants, agreements and obligations necessary to be performed by Seller under this Agreement prior to the Closing Date.

3.02. Conditions Imposed by Seller. The obligations of Seller to consummate the purchase and sale under this Agreement are subject to the satisfaction of the following conditions, each of which may be waived in writing by Seller:

(a) Purchaser shall have delivered to Seller the duly executed and acknowledged Non-Competition Agreement.

(b) Purchaser shall have delivered to Seller the initial installment of the Purchase Price in the amount of $15,000.00, less the amount of the Purchaser's payments to Seller, or for the benefit of Seller, prior to or after the date of this Agreement, in the amount to be agreed upon by Seller and Purchaser pursuant to Section 1.04(a) of this Agreement.

(c) Purchaser shall have delivered to Seller the Promissory Note, together with the duly executed and acknowledged Security Agreement.

ARTICLE IV

CLOSING DATE

4.01 Closing Date.

(a) Subject to the right of Seller and Purchaser to terminate this Agreement pursuant to Section 5.02. hereof, the Closing for the consummation of the purchase and sale contemplated by this Agreement will, unless another date is agreed to in writing by Seller and Purchaser, take place on the Closing Date.

(b) For all purposes hereof, the term "the Effective Time of Closing" shall occur upon the delivery to Purchaser of the Assignment and the Non-Competition Agreement and the other documents as contemplated herein on the Closing Date.

ARTICLE V

MISCELLANEOUS

5.01. Further Actions. From time to time, as and when requested by Purchaser or Seller, Seller or Purchaser shall execute and deliver, or cause to be executed and delivered, such documents and instruments and shall take, or cause to be taken, such further or other actions as may be reasonably necessary to effectuate the Transaction and transfer, assign and deliver to Purchaser, or Purchaser's assigns, the Assets (or to evidence the foregoing) and to consummate and to effect the other transactions expressly required to be performed by Seller hereunder.

5.02. No Broker. Seller and Purchaser represent and warrant to the other that they have no obligation or liability to any broker or finder by reason of the transactions

which are the subject of this Agreement. Each party agrees to indemnify the other party against, and to hold the other harmless from, at all times after the date hereof, any and all liabilities and expenses (including without limitation legal fees) resulting from, related to or arising out of any claim by any person for brokerage commissions or finder's fees, or rights to similar compensation, on account of services purportedly rendered on behalf of Seller or Purchaser, as the case may be, in connection with this Agreement or the transactions contemplated hereby.

5.03. Expenses. Except as otherwise specifically provided herein, Seller and Purchaser shall each bear their own legal fees, accounting fees and other costs and expenses with respect to the negotiation, execution and the delivery of this Agreement and the consummation of the transactions hereunder, and Seller will pay its expenses after the Effective Time of Closing out of the Purchase Price proceeds paid by Purchaser to Seller pursuant to Section 1.04. Purchaser shall pay all sales, transfer and documentary fees or taxes incident to the sale of the Assets, if any.

5.04. Entire Agreement. This Agreement and the Exhibits hereto are intended by the parties as a final expression of the entire agreement between Seller and Purchaser with respect to the transactions contemplated by this Agreement and supersede all prior oral or written agreements, arrangements or understandings with respect thereto.

5.05. Descriptive Headings. The descriptive headings of this Agreement are for convenience only and shall not control or affect the meaning or construction of any provision of this Agreement.

5.06. Notices. All notices or other communications which are required or permitted hereunder shall be in writing and shall be delivered either personally or by telegram, telex, telecopy or similar facsimile means, by registered or certified mail (postage prepaid and return receipt requested), or by express courier or delivery service, addressed to the addresses of the parties shown on page 1 of this Agreement or at such other address and number as either party shall have previously designated by written notice given to the other party in the manner hereinabove set forth. Notices shall be deemed given when received, if sent by telegram, telex, telecopy or similar facsimile means (confirmation of such receipt by confirmed facsimile transmission being deemed receipt of communications sent by telex, telecopy or other facsimile means); and when delivered and receipted for (or upon the date of attempted delivery where delivery is refused), if hand-delivered, sent by express courier or delivery service, or sent by certified or registered mail.

5.07. GOVERNING LAW. THIS AGREEMENT SHALL BE GOVERNED BY AND CONSTRUED IN ACCORDANCE WITH THE LAWS OF THE STATE OF TEXAS (OTHER THAN THE CHOICE OF LAW PRINCIPLES THEREOF).

5.08. Waivers and Amendments. Any waiver of any term or condition of this Agreement, or any amendment or supplementation of this Agreement, shall be effective only if in writing. A waiver of any breach or failure to enforce any of the terms or conditions of this Agreement shall not in any way affect, limit or waive a party's rights hereunder at any time to enforce strict compliance thereafter with every term or condition of this Agreement.

5.09. Illegalities. In the event that any provision contained in this Agreement shall be determined to be invalid, illegal or unenforceable in any respect for any reason, the validity, legality and enforceability of any such provision in every other respect and the remaining provisions of this Agreement shall not, at the election of the party for whose benefit the provision exists, be in any way impaired.

5.10. Counterparts. This Agreement may be executed in any number of counterparts, and each such counterpart hereof shall be deemed to be an original instrument, but all such counterparts together shall constitute but one Agreement. Facsimiles of signatures shall be deemed as original signatures.

5.11. Survival; Exclusivity of Remedies. The representations and warranties, covenants and agreements of the parties hereto shall survive the Closing.

5.12 Assignment by Purchaser. Purchaser may assign Purchaser's rights under this Agreement without restriction of any kind. Any assignee of Purchaser's rights hereunder shall succeed to all of the rights, powers, duties, benefits and obligations of Purchaser hereunder.

IN WITNESS WHEREOF, the undersigned have executed this Agreement as of the date first above written.

PURCHASER:

TEXAS PHARMACEUTICALS, INC., a Texas corporation

BY: _____

NAME: _____

TITLE: _____

DATE: 3/6/98

[SIGNATURE OF SELLER FOLLOWS ON NEXT PAGE]

SELLER:

NICHOLAS BACHYNSKY

STATE OF TEXAS §
§
COUNTY OF BEXAR §

BEFORE ME, the undersigned authority, on this day personally appeared NICHOLAS BACHYNSKY known to me to be the person whose name is subscribed to the foregoing instrument, and acknowledged to me that he executed the same for the purposes and consideration therein expressed.

GIVEN UNDER MY HAND AND SEAL OF OFFICE, this the 5th day of March, 1998.

VIRGINIA OHLENBUSCH
MY COMMISSION EXPIRES
May 4, 2000
[SEAL]

Virginia Ohlenbusch
Notary Public Signature

Virginia Ohlenbusch
Notary Printed Name
Commission Expires: 5-4-2000

STATE OF TEXAS §
§
COUNTY OF _____ §

BEFORE ME, the undersigned authority, on this day personally appeared JAMES J. NAPLES, President of TEXAS PHARMACEUTICALS, INC., a Texas corporation, known to me to be the person whose name is subscribed to the foregoing instrument, and acknowledged to me that he executed the same for the purposes and consideration therein expressed and in the capacity therein stated, as the act and deed of said corporation.

GIVEN UNDER MY HAND AND SEAL OF OFFICE, this the 6th day of March, 1998.

PATTY HAMILTON
Notary Public
State of Texas
Commission Expires 11-9-98
[SEAL]

Patty Hamilton
Notary Public Signature

PATTY HAMILTON
Notary Printed Name
Commission Expires: 11-9-98

ASSIGNMENT

DATE: March 4, 1998

ASSIGNOR: NICHOLAS BACHYNSKY
701 W. 14th Street
Texarkana, Texas 75501

ASSIGNEE: TEXAS PHARMACEUTICALS, INC., a Texas corporation
701 W. 14th Street
Texarkana, Texas 75501

In consideration of Ten Dollars ($10.00) cash in hand paid to me and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, I, NICHOLAS BACHYNSKY (hereinafter called "Assignor"), who have made an invention of a novel use and method of inducing intracellular hyperthermia and free radical flux through the use of dinitrophenol and other mitochondrial uncoupling agents in the treatment of infectious and malignant disease, assign, sell, transfer and convey to TEXAS PHARMACEUTICALS, INC., a Texas corporation, whose address is 1314 Main Street, Texarkana, Bowie County, Texas 75501 (hereinafter called "Assignee"), its successors and assigns, Assignor's entire right, title and interest in and to the following rights, interest, and property (hereinafter collectively called the "Rights"):

1. Assignor's invention of uses, methods and therapies of inducing intracellular hyperthermia and free radical flux through the use of dinitrophenol and other mitochondrial uncoupling agents in the treatment of infectious and malignant disease, including without limitation Assignor's rights, powers, interests and title in and to the methods, uses and processes described in Schedule 1 attached to this Assignment, (collectively, herein called the "Invention").

2. All applications for patent or like protection on said Invention that have been

or may in the future be made by Assignor or Assignor's legal representatives, in any and all countries.

3. All patents and like protection that have been or may in the future be granted on said Invention to Assignor or Assignor's legal representatives, in any and all countries of the world.

4. All substitutions for and divisions, continuations, continuations-in-part, renewals, reissues, extensions and the like of said applications and patents and similar rights or grants, including, without limitation, those obtained or permissible under past, present and future law and statutes.

5. All rights of action on account of past, present and future authorized or unauthorized use of said Invention and for infringement of said patents and like protection.

6. The right of Assignee to file in his name disclosure documents, applications for patents and like protection for said Invention in any country and countries in the world.

7. All international rights of priority associated with said Invention, disclosure filings, applications, patents and like protection.

TO HAVE AND TO HOLD the Rights unto the Assignee, its successors and assigns forever, and Assignor does hereby bind himself, his heirs, legal representatives and assigns, to forever WARRANT and DEFEND the title to the Rights unto the said Assignee, its successors and assigns, against any person whomsoever lawfully claiming, or to claim the same, or any part thereof.

Assignor covenants and agrees that Assignor will cooperate with Assignee such that Assignee may enjoy to the fullest extent the benefit of this Assignment. Such cooperation shall include, but not limited to, all of the following:

1. Assignor's prompt execution of all papers that are deemed necessary or desirable by Assignee to perfect the right, title and interest herein conveyed, and

2. Assignor's prompt execution of all petitions, oaths, specifications, declarations

or other papers that are deemed necessary or desirable by Assignee for filing and prosecuting patent applications, for filing and prosecuting substitute, division, continuing, or additional applications in the United States and/or all foreign countries, for filing and prosecuting applications for reissuance or reexamination of letters patent, and for interference proceedings involving and covering any of the Rights, and

3. Assignor's prompt assistance and cooperation, including but not limited to execution of documents and testifying, in the prosecution of legal proceedings involving any of the Rights, including, but not limited to, patent prosecution, interference proceedings, infringement court actions, opposition proceedings, cancellation proceedings, priority contests, unfair competition court actions, trade secret court actions, public use proceedings, slander, license breach and royalty collection proceedings and other legal proceedings.

Assignor warrants that Assignor has the right to make the assignment set forth herein and that no other person or entity has any rights of ownership or claim to the subject matter of this Assignment. This Assignment is binding upon Assignor, Assignor's heirs, administrators, executors, successors, trustees, devisees and assigns and inures to and for the benefit of Assignee, its successors and assigns.

EXECUTED effective as of the date first above written and at the time and place indicated below opposite the signature:

Nicholas Bachynsky

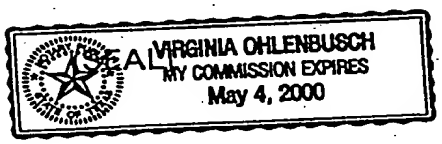
NICHOLAS BACHYNSKY

Date: 3/4/98

STATE OF TEXAS §
§
COUNTY OF BEXAR §

BEFORE ME, the undersigned authority, on this day personally appeared NICHOLAS BACHYNSKY known to me to be the person whose name is subscribed to the foregoing instrument, and acknowledged to me that he executed the same for the purposes and consideration therein expressed.

GIVEN UNDER MY HAND AND SEAL OF OFFICE, this the 5th day of March, 1998.



Virginia Ohlenbusch
Notary Public Signature

Virginia Ohlenbusch
Notary Printed Name

Commission Expires: 5-4-2000

SCHEDULE 1 TO ASSIGNMENT

INVENTION

This invention provides a medical method for: (1) prevention of life threatening hypothermia; (2) enhancing magnetic resonance spectroscopy and positron emission tomographic metabolic imaging; and (3) treatment of resistant neoplastic and infectious disease by concurrent administration of dinitrophenol [or other mitochondrial thermoregulatory uncoupling agents, e.g., carbonylcyanide m-chorophenylhydrazone (CCCP), carbonylcyanide-p-trifluoromethoxy-phenylhydrazone (FCCP), recombinant brown fat type protein, or lipid proton ionophores] and respiratory oxygen, intravenous fluids, anti-platelet drugs, as needed cooling, and specific metabolic, activating cytokines [e.g., recombinant tumor necrosis factor (TNF), interferons, etc.], hormones (e.g., glucagon), and other medications to control and focally enhance the mitochondrial uncoupling effects.

The present invention avoids the use of labor intensive, complex hyperthermia equipment, including invasive extracorporeal perfusion, with its associated thermal gradient toxicity problems to interposed normal tissues, inherent to all therapeutic methods of delivering heat from the outside-in. A new use(s)/method of generating intracellular oxygen derived free radicals, and heating from within the cell has been discovered for dinitrophenol (or other oxidative phosphorylation uncouplers) in prevention of cold injury, and treatment of free radical-thermosensitive parasites (e.g., Echinococcus), bacteria (e.g., Borrelia burgdorferi), lipid enveloped viruses (e.g., HIV), and neoplasia (e.g., gastric adenocarcinoma). It has further been discovered that cataracts, induced by dinitrophenol in the treatment of chronic obesity, can be prevented by concomitant administration of a variety of free radical scavenging agents, including tocopherol, ascorbic acid, and beta-carotene.

Briefly, the present invention is a new use(s)/method of inducing increased, intracellular free radical flux and hyperthermia, including the procedure of administrating dinitrophenol to patients in doses sufficient to denature and inactivate targeted biologic systems. Concurrent administration of tissue selective activating hormones, biologicals or drugs permits greater enhancement of the therapeutic index, while physiologic gain cooling, fluids, respiratory oxygen, and monitoring procedures permit safe therapeutic control. The figure on the attached page depicts an example use(s)/methodology of this process in an algorithm.

SCHEMATIZED MITOCHONDRIAL UNCOUPLING METHOD FOR DIAGNOSIS OR TREATMENT OF INFECTIOUS AND MALIGNANT DISEASE

ORGANISM or MALIGNANCY — **PATIENT**

TREATMENT EVALUATION

BIOLOGIC CRITERIA

* Confirmed Diagnosis by culture, PCR, or histopathology; specific serology.
* Known Temperature and Heating Time required for inactivation, e.g., Treponema pallidum (syphilis)-41.5°C @ 1 hour; Borrelia burgdorferi (Lyme Disease)-41.5°C @ 1 hour; Echinococcus multilocularis (Hydatid infestation)-41°C @ 15 minutes; HIV, chronically infected (provirus) cells (tissue culture)-42°C @ 10 hours, with recombinant TNF-a, 42°C @ 3 hours. Kaposi's sarcoma, HIV infection in the patient-42°C @ 2 hours/44°C @ 15 minutes.
* Unknown Temperature and Heating Time required for inactivation of neoplasms, or other infectious agents, determined by predictive - assay of biopsy/culture; generally, treatment temperature/time will be decreased due to endogenous uncoupling also occurring in targeted biologic system (except viral).

CLINICAL CRITERIA

* History of cardiac, hepatic, pulmonary renal, CNS, malignant hyperthermia, or endocrine disease, i.e., exclusion of patients-congestive heart failure, severe dysrhythmias; alcoholic or other hepatitis with elevated bilirubin/enzymes; known endocrinopathies of brittle diabetes, pheochromocytoma, etc.; medications known to stimulate the physiologic response of hypermetabolic state and hyperthermia, e.g., vascular constrictors, anticholinergics, calcium channel blocker, etc.
* Pulmonary, renal, hepatic function tests; chest X-ray; CBC with platelet count; Chem profile with Ca^{++}, Mg^{++}, $PO_4^{=}$; exercise-multigated cardiac radionucleotide scan with resting ejection fraction of at least 45%, and no deterioration upon exercise.
* Enhancing or sensitizing agents to increase therapeutic gain, i.e., use of ionizing radiation, chemotherapy, drugs, or biologic modifiers (synergistic or additive).

METHOD PROTOCOL

TREATMENT

* Dinitrophenol, dosage & schedule on "Biologic/Clinical Criteria"; IV (or IM-SC) test dose (1mg/kg) by VO_2 response-1ml O_2/sec=20watts; common IV dosage, 1-5mg/kg, q 1-4 hr, PO 2X greater q 6-12 hr; BMR & heat dissipation modify dose/schedule.
* Other mitochondrial uncoupling agents, increased potency/more localized effect, e.g., FCCP, CCCP, perfluorooctane sulfonamide, SF-6847; long chain fatty acids, and brown fat "thermogin", etc.
* Modulating-controlling agents, tissue specific mediators which modulate substrate turnover rates through Krebs cycle; glucagon, .5-10mg/hr-IV; dopamine(1-10 micrograms/kg/min); insulin-dose based on blood glucose; dobutamine(1-15 micrograms/kg/min); amrinone(5-7.5 micrograms/kg/min); isoproterenol (.5-2 micrograms/min).

BASELINE & MONITORED

* Oxygen consumption/increase, precedes core temperature increase by 4 minutes; prolonged or high risk patient-additional monitoring of tissue oxygenation by gastric pH, NMR, PET or infrared spectroscopy, ear oximetry, blood gas.
* Core temperature, esophageal, rectal, bladder catheter thermistors.
* Cardiac function, continous display of rhythm, rate, blood pressure and respiratory rate; Swan-Ganz catheter for high risk patient.
* Renal output/function, maintain at least 1-1.5ml per kg /hour; observe for possible myoglobinuria and monitor fluid input/output.
* Hepatic function tests, at target temperature; iosoenzyme fractionation if tumor lysis is a consideration.
* CNS agitation, anxiety, possible seizure prophylaxis.
* Blood chemistry/electrolytes-glucose, $PO_4^{=}$, serum creatinine.

MANAGEMENT

* Oxygen (100%) @ 4-6 liters/minute via nasal cannula/face mask.
* Heat control with evaporation preventing-water absorbing blankets/plastic liners; cooling control-if needed with tepid H_2O spray and/or fan evaporative loss; use of P.O. propylthiouracil (PTU); Decadron-I.V.
* Intravenous fluids, i.e., .85% Saline, D_5W-½NS, supplemented with appropriate milliequivalents of K^+, $PO_4^{=}$, Mg^{++}; fluid rate to compensate for evaporative and urinary losses, maintain BP.
* Arrhythmia control, if needed-use of non-negative inotropic, or drugs that cannot cause cardiac decompensation in hypermetabolic state e.g., lidocaine; avoidance of beta blockers and Ca^{++} channel blockers.
* Anxiety, possible seizure control with I.V. valium, thiopental; avoidance of drugs with atropine like effects or major anti-psychotic drugs.

MEDICAL USES

DNP-IV @ 1mg/kg (2X-VO_2) → **DIAGNOSIS** – Enhancement of NMR, PET, & Near-Infrared Spectroscopy. → Sensitivity increased by enhanced metabolic difference between diseased/normal tissues, i.e., O_2, glucose, fatt acid, ATP, phosphocreatine & specific substrate consumption; lactic acid, free radical production; early diagnc & predictability of disease treatment parameters/succe

DNP-IV @ 2-5mg/kg q3-6hr for 2X-VO_2 → **THERAPY OF INFECTIOUS & MALIGNANT DISEASE** (dosage/frequency of uncoupling agent will be determined by the specific agent created & use of modulating, enhancing, or other combined therapy drugs.

- → PARASITIC (See Illustrative Example)
- 41.5°C/1 hr (or less) → BACTERIAL (Borrelia burgdorferi)
- 42°C/2 to 8 hrs (or less) → VIRAL (HIV)
- Based on predictive biopsy and use of radiation, chemotherapy or biologic response modifiers → NEOPLASTIC

ILLUSTRATIVE METHOD/USE EXAMPLE [1/]

A 52 year old white Swiss [redacted]e, hunting dog trainer, presente[redacted]th right upper quadrant abdominal pain. History revealed past(24 month old) hepatic "cyst" surgery and treatment with albendazole(only 1 dose was given because of anaphylactic reaction). He denied history of weight loss, pulmonary, cardiac or neurologic disease. Upon physical examination, he had a weight of 198 pounds (90 Kg), height of 5'11", blood pressure 140/80, pulse-76 and regular, respirations 18/minute, and oral temperature of 37.3°C. Laboratory studies, including hepatic, renal, pulmonary and cardiac function tests were normal; complete blood count was unremarkable except for 20% eosinophilia. Ultrasound and nuclear magnetic resonance of the liver revealed 4 (2-3 cm. in diameter) cysts in the mid-right lobe; ELISA serology showed a diagnostic titer specific for Hydatid disease with Echinococcus multilocularis. The patient refused to entertain any additional surgery or albendazole therapy.

After clinical assessment and treatment evaluation, i.e., Echinococcus multilocularis protoscoleces and germinal layers are destroyed at 41°C/15 minutes, whereas liver-hepatocytes withstand temperatures of 42°C to 44°C for known periods of 20 hours and 15 minutes respectively, the patient was given 1 aspirin; 10 mg. diazepam by mouth; and, intravenous fluids of 0.85 normal saline containing 9 millimolar K_2PO_4, 7 milliequivalents of K^+, and 2cc of 50% saturated solution of Mg_2SO_4/liter, were infused at a rate of 12cc/kg/hr. Urine output was maintained at 1cc/kg/hour or greater. Esophageal (optional), rectal and foley (16 gauge) tipped bladder catheter thermistors gave temperature readings every two minutes within 0.1°C. Cardiac rate, rhythm, blood pressure, and repiratory rate sensors were placed and continously displayed on a multichannel monitor. Intravenous glucagon-2mg/hr was infused, with 1 mg given prior to DNP.

The patient was covered with a water absorbing polyethelene lined blanket, and baseline respiratory gas flow/oxygen consumption (VO_2) was determined using a 3 minute bag collection. Five minutes after intravenous administration of 90 mg of dinitrophenol (2% DNP/5% $NaHCO_3$ at 1 mg/kg), and determination that there was no untoward or idiosyncratic reaction, an additional 90 mg of 2,4 dinitrophenol (total of 180mg, 2mg/kg body weight) was infused. Monitored physiologic parameters are shown in the Table below. An additional VO_2 rate was obtained five minutes after the second dose of DNP and the patient was thereafter placed on 100% O_2 via nasal canula. Target core temperature was maintained by occasional exposure of a limb and/or decreasing the glucagon infusion rate to 0.25 mg/hour. After the patient was maintained at a core temperature of 41.3°C for 20 minutes, the treatment was terminated by removing the blanket and permitting evaporative and radiant heat loss to return the body temperature to a normothermic level.

TABLE

Monitored Clinical Data On Mitochondrial Uncoupling Use/Method In Illustrative Example
(Treatment of Hydatid disease-Echinococcus multilocularis)

Time (minutes)	Medication (type & dose)	Resp. Rate-O_2 Consumption (breaths/min)	(O_2 ml/min)	Cardiac Rate (beats/min)	Urine Output (total ml)	Core Temp. (°C)	Other (remarks)
-60	I.V. Fluids - .85% NS @ 0.8 L/hour	18	290	78	-	37.1	Fluids @ 10-12cc per kg/hour.
-30	Glucagon-IV Drip @ 2mg/hour	20	-	78	47	37.1	Hepatic Krebs Cycle stimulation.
0	2,4-dinitrophenol-90mg IV in 4.5ml of 5%$NaHCO_3$	20	-	88	58	37.4	Covered with polyethylene blanket.
2	[prepared by dissolving 2.0gm DNP(15% H_2O) in 5% $NaHCO_3$-giving 2% solution)	24	350	92	-	37.8	Increased O_2 consumption precedes temp. elevation.
5	2,4-dinitrophenol-90mg IV in 4.5ml of 5%$NaHCO_3$	26	-	98	-	37.8	
10	Fluids increased to 1.2 L/hour; start O_2	30	680	110	15	39.4	After VO_2 determined 100% O_2 @ 4 L/min via nasal cannula.
20	-	30	-	120	18	40.3	
40	Glucagon -IV Drip decreased to 0.5mg/hr	30	-	138	28	41.4	Lower extremity is partially exposed.
60	Glucagon discontinued	30	-	140	30	41.2	Blanket removed
120	IV fluid discontinued	24	-	100	98	38.4	All thermistors removed

1/ Variations of the above use/method, i.e., protocol evaluation, monitoring, medications/dosages, time & temperature of mitochondrial uncoupling, will be necessitated by clinical and targeted biologic system treatment factors. Such variations for treatment of other parasitic (e.g. Malaria), bacterial (e.g., Lyme, Hansons disease), viral (e.g., HIV) and neoplastic disease will occur to those skilled in the art of medicine, and will be more fully described in the patent application.

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

OCTOBER 16, 2001

PTAS

101863153A

FULBRIGHT & JAWORSKI LLP
DAVID L. FOX
1301 MCKINNEY
SUITE 5100
HOUSTON, TX 77010-3095

UNITED STATES PATENT AND TRADEMARK OFFICE
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

THE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF THE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS AVAILABLE AT THE ASSIGNMENT SEARCH ROOM ON THE REEL AND FRAME NUMBER REFERENCED BELOW.

PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE INFORMATION CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA PRESENT IN THE PATENT AND TRADEMARK ASSIGNMENT SYSTEM. IF YOU SHOULD FIND ANY ERRORS OR HAVE QUESTIONS CONCERNING THIS NOTICE, YOU MAY CONTACT THE EMPLOYEE WHOSE NAME APPEARS ON THIS NOTICE AT 703-308-9723. PLEASE SEND REQUEST FOR CORRECTION TO: U.S. PATENT AND TRADEMARK OFFICE, ASSIGNMENT DIVISION, BOX ASSIGNMENTS, CG-4, 1213 JEFFERSON DAVIS HWY, SUITE 320, WASHINGTON, D.C. 20231.

RECORDATION DATE: 07/21/2000

REEL/FRAME: 012063/0015
NUMBER OF PAGES: 8

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:
BACHYNSKY, NICHOLAS

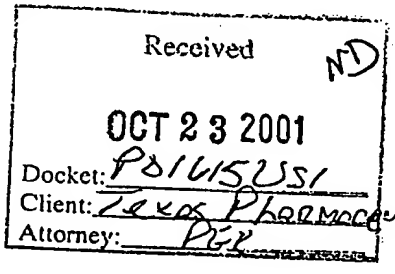
DOC DATE: 03/04/1998

ASSIGNEE:
TEXAS PHARMACEUTICALS, INC.
701 W. 4TH STREET
TEXARKANA, TEXAS 75501

SERIAL NUMBER: 09744622
PATENT NUMBER:
PCT NUMBER: US9916940

FILING DATE:
ISSUE DATE:

STEVEN POST, EXAMINER
ASSIGNMENT DIVISION
OFFICE OF PUBLIC RECORDS



Form PTO-1595
(Rev. 6-93)
OMB No. 0651-0011 (exp. 4/94)

10-16-2001

101863153

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

RECORDATION SHEET

To the Honorable Commissioner of Patents and Trademarks:
Please record the attached original documents or copy thereof.

1. Name of conveying party(ies):
Nicholas Bachynsky

Additional name(s) of conveying party(ies) attached?
☐ Yes ☒ No

MRD
7-21-00

2. Name and address of receiving party(ies):

Name: Texas Pharmaceuticals, Inc.

Internal Address:

Street Address: 701 W. 4th Street

City: Texarkana

State: TX Zip: 75501

3. Nature of Conveyance:

☒ Assignment ☐ Merger

☐ Security Agreement ☐ Change of Name

☐ Other

Execution Date: March 4, 1998

Additional name(s) & address(es) attached?
☐ Yes ☒ No

4. Application number(s) or patent number(s): PCT/US99/16940

If this document is being filed together with a new application, the execution date of the application is:

A. Patent Application No.(s):

B. Patent No.(s)

Additional numbers attached? ☐ Yes ☒ No

5. Name and address of party to whom correspondence concerning document should be mailed:

Name: David L. Fox

Internal Address: Fulbright & Jaworski LLP

Street Address: 1301 McKinney

Suite 5100

City: Houston

State: TX Zip: 77010-3095

6. Total number of applications and patents involved: 1

7. Total fee (37 CFR 3.41): ..... $ 40.00

☒ Enclosed

☐ Authorized to be charged to deposit account

8. Deposit account number: 40E

(Attach duplicate copy of this page if paying by deposit account)

DO NOT USE THIS SPACE

9. Statement and signature.
To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is a true copy of the original document.

David L. Fox
Name of Person Signing

Signature

17 July 2000
Date

Total number of pages including cover sheet, attachments, and document: 8

10/11/2001 PVOLPE 00000003 PCT/US99/16940
01 FC:581 40.00 OP

Mail documents to be recorded with required cover sheet information to:
Commissioner of Patents & Trademarks, Box Assignments
Washington, D.C. 20231

Received
OCT 23 2001

Docket:
Client:
Attorney:

NON-COMPETITION AGREEMENT

THIS NON-COMPETITION AGREEMENT (this "Agreement") dated as of March 4, 1998, is by and between **NICHOLAS BACHYNSKY**, whose address for the purposes of this Agreement is 701 W. 14th Street, Texarkana, Bowie County, Texas 75501 (the "Seller") and **TEXAS PHARMACEUTICALS, INC.**, a Texas corporation, whose address for the purposes of this Agreement is 701 W. 14th Street, Texarkana, Bowie County, Texas 75501 (the "Purchaser").

RECITALS:

A. Seller and Purchaser have entered into an Agreement For Sale of Invention and Related Rights dated as of March 2, 1998 (the "Sales Agreement") pursuant to which, among other things, Purchaser has agreed to purchase from Seller, and Seller has agreed to sell to Purchaser, certain assets of Seller described therein, including (without limitation) Seller's invention of a use and method of inducing intracellular hyperthermia and free radical flux through the use of dinitrophenol and other mitochondrial uncoupling agents in the treatment of infectious and malignant disease (the "Invention") and all rights of Seller under any and all disclosure documents, patents and patent applications relating thereto in all countries of the world and all other rights related to the Invention (the "Assets").

B. Seller possesses certain confidential information relating to the Invention which is proprietary in nature and which is not and will not be generally disclosed. To induce Purchaser to enter into the Sales Agreement and to purchase Seller's Assets, Seller has agreed to enter into this Agreement to assure Purchaser that Seller will not use Seller's confidential information in a manner which will injure the commercial value of the Invention or the Assets.

NOW, THEREFORE, in consideration of the premises and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Seller and Purchaser hereby covenant and agree as follows:

1. Covenant Not To Compete. Seller hereby covenants that commencing upon the date hereof and continuing until November 1, 2005, Seller shall not, unless acting as an employee or licensee of the Purchaser, own, manage, operate, join, control or participate in, directly or indirectly, or derive any benefits whatever from, or be an officer, director, employee, partner, agent, consultant or shareholder of, any business engaged in any activity that is in "Competition" in any manner whatsoever with the business of Purchaser in the "Specified Geographical Area," and Seller shall not render assistance or advice to any person, firm or enterprise which is so engaged. For purposes of this paragraph,

(a) "Competition" means the treatment of patients using methods covered by the Invention or otherwise using dinitrophenol or other mitochondrial uncoupling agents; and

(b) "Specified Geographical Area" means the United States of America and any location in any country in which Purchaser holds a patent or patent application upon the Invention.

2. Payments in Consideration of Covenant Not To Compete. In consideration of the covenants of Seller set forth in paragraph 1 above, Purchaser has purchased from Seller the Assets for the consideration set forth in the Sales Agreement.

3. Entire Agreement. This Agreement constitutes the entire agreement between the parties hereto with respect to the subject matter of this Agreement and supersedes and is in full substitution for any and all prior agreements and understandings whether written or oral between said parties relating to the subject matter of this Agreement, except as set forth in the Sales Agreement.

4. Amendment. This Agreement may not be amended or modified in any respect except by an agreement in writing executed by the parties in the same manner as this Agreement.

5. Assignment. This Agreement may be assigned without the consent of Seller in connection with the sale, transfer or other assignment of all or substantially all of the assets acquired by the Purchaser from the Seller under the Sales Agreement.

6. Heirs and Successors. This Agreement shall be binding upon and shall inure to the benefit of and be enforceable by each of the parties and their respective heirs, legal representatives, successors and assigns.

7. Invalid Provisions. If any provision of this Agreement is held to be illegal, invalid or unenforceable under present or future law effective during the term hereof, such provision shall be fully severable. This Agreement shall be construed and enforced as if such illegal, invalid or unenforceable provision had never comprised a part hereof and the remaining portions hereof shall remain in full force and effect and shall not be effected by the illegal, invalid or unenforceable provision or by its severance herefrom. Furthermore, in lieu of such illegal, invalid or unenforceable provision there shall be added automatically as part of this Agreement a provision similar in terms to such illegal, invalid or unenforceable provision as may be possible and be legal, valid and enforceable.

8. Specific Performance. Seller acknowledges that Seller's breach of the provisions of Section 1 of this Agreement will cause irrevocable harm to Purchaser, for which there may be no adequate remedy at law and for which the ascertainment

of damages would be difficult. Therefore, Purchaser will be entitled, in addition to, and without having to prove the inadequacy of, other remedies at law (including without limitation damages for prior breaches hereof), to specific performance of this Agreement, as well as injunctive relief (without being required to post bond or other security).

9. Notice. All notices, consents, requests, approvals or other communications in connection with this Agreement and all legal process in regard hereto shall be in writing and shall be deemed validly delivered, if delivered personally or sent by certified mail, postage prepaid. Unless changed by written notice pursuant hereto, the address of each party for the purposes hereof is the address set forth on page 1 of this Agreement. Notice given by mail shall be deemed delivered only when actually received.

10. Descriptive Headings. The descriptive headings of the several sections of this Agreement are inserted for convenience only and shall not control or affect the meaning or construction of any of the provisions hereof.

11. GOVERNING LAW. THIS AGREEMENT SHALL BE GOVERNED BY AND CONSTRUED AND ENFORCED IN ACCORDANCE WITH THE LAWS OF THE STATE OF TEXAS (OTHER THAN THE CHOICE OF LAW PRINCIPLES THEREOF).

IN WITNESS WHEREOF, the parties have duly executed this Non-Competition Agreement as of the date first above written.

SELLER:

NICHOLAS BACHYNSKY

PURCHASER:

TEXAS PHARMACEUTICALS, INC., a Texas corporation

BY: _____
NAME: _____
TITLE: _____

DATE: 3/6/98

PROMISSORY NOTE

DATE: March 2, 1998

MAKER: TEXAS PHARMACEUTICALS, INC., a Texas corporation

MAKER'S MAILING ADDRESS: 701 W. 14th Main Street
Texarkana, Texas 75501

PAYEE: NICHOLAS BACHYNSKY

PLACE FOR PAYMENT: 701 W. 14th Street, Texarkana, Bowie County, Texas 75501

PRINCIPAL AMOUNT: THIRTY-FIVE THOUSAND DOLLARS US ($35,000.00 US)

ANNUAL INTEREST RATE ON UNPAID PRINCIPAL FROM DATE: Six and one-half percent (6½%)

ANNUAL INTEREST RATE ON MATURED, UNPAID AMOUNTS: Ten percent (10%)

TERMS OF PAYMENT (PRINCIPAL AND INTEREST): All principal and interest hereunder shall only be due and payable upon the earlier to occur of (1) ninety (90) days after the date upon which Maker has obtained a United States Patent upon the use and method described as the Invention in the Agreement For Sale of Invention and Related Rights between Maker and Payee, of even date herewith, or (2) March 1, 2002. Payments will be credited first to the accrued interest and then to reduction of principal.

SECURITY FOR PAYMENT: This note is secured by a purchase money security interest granted in Security Agreement of even date herewith executed by Payee, as secured party, and Maker, as debtor.

Maker promises to pay to the order of Payee at the place for payment and according to the terms of payment the principal amount plus interest at the rates stated above.

If Maker defaults in the payment of this note or in the performance of any obligation in any instrument securing or collateral to it, and the default continues after Payee gives Maker notice of the default and the time within which it must be cured, as may be required by law or by written agreement, then Payee may declare the unpaid principal balance and earned interest on this note immediately due and payable. Maker and each surety, endorser and guarantor waive all demands for payment,

presentations for payment, notices of intention to accelerate maturity, notices of acceleration of maturity, protests, and notices of protest, to the extent permitted by law.

If this note or any instrument securing or collateral to it is given to an attorney for collection or enforcement, or if suit is brought for collection or enforcement, or if it is collected or enforced through probate, bankruptcy, or other judicial proceeding, then Maker shall pay Payee all costs of collection or enforcement, including reasonable attorney's fees and court costs, in addition to other amounts due. Reasonable attorney's fees shall be ten percent (10%) of all amounts due unless either party pleads otherwise.

Interest on the debt evidenced by this note shall not exceed the maximum amount of non-usurious interest that may be contracted for, taken, reserved, charged or received under law; any interest in excess of that maximum amount shall be credited on the principal of the debt or, if that has been paid, refunded. On any acceleration or required or permitted prepayment, any such excess shall be canceled automatically as of the acceleration or prepayment or, if already paid, credited on the principal of the debt or, if the principal of the debt has been paid, refunded. This provision overrides other provisions in this and all other instruments concerning the debt.

Each Maker is responsible for all obligations represented by this note. When the context requires, singular nouns and pronouns include the plural.

In the event default occurs in the timely and prompt payment of all or any part of the indebtedness evidenced by this note, any judicial proceedings against Maker shall be limited to the preservation, enforcement and foreclosure of the liens, rights, properties and estates of the Security Agreement securing this note, and Maker shall have no personal liability for the repayment of this note. No attachment, execution or other writ of process shall be sought, issued or levied upon any assets, properties or funds of Maker or any agent, employee or other person or entity affiliated with the Maker.

MAKER:

TEXAS PHARMACEUTICALS, INC., a Texas corporation

BY: _____

NAME: _____

TITLE: _____

SECURITY AGREEMENT

This SECURITY AGREEMENT (this "Agreement") is made effective this 4th day of March, 1998, by and between **TEXAS PHARMACEUTICALS, INC., a Texas corporation**, whose address is 701 W. 14th Street, Texarkana, Bowie County, Texas 75501 (the "Borrower") and **NICHOLAS BACHYNSKY**, an individual whose address for the purposes of this Agreement is 701 W. 14th Street, Texarkana, Bowie County, Texas 75501 (the "Secured Party").

RECITALS:

A. This Agreement is being executed in connection with Secured Party's agreement to sell, and Borrower's agreement to purchase certain property, a portion of the purchase price of which is evidenced by that certain Promissory Note of even date herewith in the principal sum of $35,000.00, executed by Borrower and payable to Secured Party. Such transaction is more particularly described in that certain Agreement For Sale of Invention and Related Rights dated as of March 2, 1998, between Secured Party, as seller, and Borrower, as purchaser (herein, the "Sales Agreement").

B. As inducement to Secured Party to consummate the sale described in the Sales Agreement and to accept as part of the consideration for such sale the Promissory Note, Borrower is simultaneously herewith providing a security interest in Borrower's right, title and interest in and to the Collateral Security (hereafter described) to Secured Party.

AGREEMENT:

NOW THEREFORE, in consideration of the foregoing and for other good and valuable consideration, receipt of which is hereby acknowledged, Borrower and Secured Party hereby agree as follows:

Section 1. Definitions. The following terms shall have the definitions set forth below:

"Code" shall mean the Uniform Commercial Code as adopted in the State of Texas as the Business and Commerce Code, as amended from time to time.

"Collateral Security" shall mean the collateral described in Section 4 hereof.

"Effective Date" shall mean the date hereinabove first set forth.

"Event of Default" shall mean any condition or occurrence defined as an Event of Default in Section 8 hereof.

"Promissory Note" shall mean that certain Promissory Note of even date herewith in the principal sum of $35,000.00, executed by Borrower and payable to Secured Party.

"Obligation" is defined in Section 3 hereof.

"Potential Default" shall mean an event or occurrence which, with notice or the passage of time, or both, would constitute an Event of Default hereunder or under any of the Financing Documents.

"Security Interest" is defined in Section 2 hereof.

All other capitalized terms not defined in this Section 1 shall have the meaning set forth for such terms elsewhere in this Agreement. In the definitions set forth herein the plural includes the singular, and the use of the singular includes the plural.

Section 2. Security Interest.

(a) Borrower hereby grants to Secured Party security interests in and to all of the Collateral Security to secure the payment and performance of the Obligation; such security interests are in addition to, and not in lieu of, any other security interest granted, now or hereafter, by Borrower to Secured Party.

(b) The security interests granted herein by Borrower are collectively referred to as the "Security Interest."

Section 3. Obligation. This Security Agreement and the Security Interest granted hereby secure the payment and performance of the monetary obligations of Borrower (in the capacity of Maker) under the Note.

Section 4. Collateral Security; Duty to Supplement Collateral Security.

(a) The Security Interest granted hereby by Borrower shall cover the following collateral:

(i) All of Borrower's right, title and interest in and to the following rights, interest, and property acquired from Secured Party pursuant to the Sales Agreement or related thereto:

(1) the uses, methods and therapies of inducing intracellular hyperthermia and free radical flux through the use of dinitrophenol and other mitochondrial uncoupling agents in the treatment of infectious and malignant

disease (the "Invention");

(2) Borrower's rights, powers, interests and title in the methods, uses, procedures, protocols and other matters contained in, related to or arising in connection with the subject matter of or otherwise related to said Invention;

(3) All applications for patent or like protection on said Invention by Borrower or Borrower's legal representatives, in any and all countries.

(4) All patents and like protection hereafter granted on said Invention to Borrower or Borrower's legal representatives, in any and all countries of the world.

(5) All substitutions for and divisions, continuations, continuations-in-part, renewals, reissues, extensions, and the like of said applications and patents and like grants, including, without limitation, those obtained or permissible under past, present and future law and statutes.

(6) All rights of action on account of past, present and future authorized or unauthorized use of said Invention and for infringement of said patents and like protection.

(7) All international rights of priority associated with said Invention, disclosure filings, applications, patents and like protection.

(b) All of the collateral described in this Section 4 is collectively referred to as the "Collateral Security."

(c) The provisions of this Security Agreement shall not be construed to permit the sale, assignment, anticipation, encumbrance or other hypothecation or disposition in any manner of the Collateral Security or any interest therein until the Obligation shall have been satisfied in full.

(d) Absent both an Event of Default and a Potential Default hereunder, and subject to the provisions of Section 7 concerning payment of certain fees and expenses authorized by this Security Agreement, Borrower shall have the right to receive and own free of any security interest hereunder all income, revenue and benefits accruing from the Collateral Security.

Section 5. [intentionally omitted]

Section 6. Representations and Warranties of Borrower. Borrower hereby represents, warrants and covenants that upon execution of this Security Agreement and at all times subsequent thereto:

(a) Except for the Security Interest granted hereby, to the best of Borrower's actual knowledge, Borrower owns the Collateral Security free from any lien, security interest, claim or encumbrance.

(b) Borrower has all requisite corporate power to enter into this Security Agreement and any and all other documents executed in connection herewith and to pledge the Collateral Security.

(c) This Security Agreement and any and all other documents executed in connection herewith constitute and shall constitute the legal, valid and binding obligation of Borrower enforceable in accordance with the terms thereof.

Section 7. Borrower's Covenants. Borrower further represents, warrants, agrees and covenants that:

(a) Borrower, upon request of Secured Party, will execute, cause to be acknowledged and deliver any and all further documents to effect the agreements herein contained, and to preserve and protect the Collateral Security and the Security Interest and to cause to be delivered to Secured Party the Collateral Security upon the occurrence of an Event of Default hereunder, as set forth in Section 8; and

(b) Borrower will reimburse to Secured Party all reasonable costs incurred by Secured Party in the enforcement of this Security Agreement following an Event of Default hereunder, as set forth in Section 8.

Section 8. Events of Default. Borrower shall be in default under this Security Agreement upon the occurrence of any of the following events or conditions expressly set forth below (each herein an "Event of Default"):

(a) an event of default of Borrower shall occur under the Note; or

(b) Borrower shall default in the timely performance of any obligation, covenant, agreement or liability contained herein.

Section 9. Remedies of Secured Party Upon Event of Default.

(a) At any time after the occurrence of an Event of Default hereunder, Secured Party, may, at its option, do any or all of the following:

(i) Exercise any or all of Secured Party's rights and remedies under this Security Agreement or under the Code with respect to all or any portion of the Collateral Security;

(ii) Exercise any and all of the rights and remedies provided to a secured creditor by the Code or at law or in equity;

(iii) Terminate Borrower's rights, if any, to possess and exercise any rights in and to the Collateral Security. If Secured Party exercises this remedy, it may do all things which, in Secured Party's discretion, are necessary for the administration or preservation of the Collateral Security without notice to or approval by Borrower.

(b) In the collection and enforcement of Collateral Security, Secured Party is hereby irrevocably and fully empowered by Borrower, as its agent and attorney-in-fact, to (i) sue in Borrower's name or in the name of Secured Party or in the name of any nominee of Secured Party with respect to the Collateral Security pledged hereunder, and (ii) exercise and enforce any and all rights of Borrower and/or Secured Party relating to the Collateral Security.

Section 10. Parties Bound. The rights of an benefits to Secured Party under this Security Agreement shall inure to the benefit of its heirs, legal representatives and assigns. The terms of this Security Agreement shall be binding upon the heirs, legal representatives and assigns of the parties hereto. All representations, warranties and agreements of Borrower shall bind Borrower's heirs, legal representatives and assigns. All references herein to Borrower or to Secured Party shall be deemed to include their respective heirs, legal representatives and assigns.

Section 11. Notices. All notices, advices, demands, requests, consents, statements, satisfactions, waivers, designations, refusals, confirmations or denials given pursuant to, or in connection with, this Security Agreement must be in writing, be either personally served, sent via overnight courier, telecopied, or sent with return receipt requested by registered or certified mail with postage (including registration or certification charges) and be addressed as set forth in the first sentence of this Agreement, or to any such other person or at such other place as Borrower or Secured Party may form time to time designate by written notice to the other.

Any matter so served upon or sent to Secured Party or Borrower in the manner aforesaid, shall be deemed sufficiently given for all purposes hereunder on the date the same was sent via overnight courier, personally delivered, or telecopied, or on the third (3rd) business day after the same shall have been deposited in a United States Post Office, except that notices of changes of address shall not be effective until actual receipt. Where no longer notice period is expressly required hereunder, notice so given at least five (5) days prior to the related action (or if the Uniform Commercial Code elsewhere specifies a longer period, such longer period) shall be deemed reasonable.

Section 12. Modifications. No provision hereof shall be modified or limited except by a written agreement expressly referring hereto and to the provision so modified or limited and signed by both parties to this Security Agreement, nor by course of conduct, usage of trade or by the law merchant.

Section 13. Severability. The unenforceability of any provision of this Security Agreement shall not affect the enforceability or validity of any other provision hereof.

Section 14. Financing Statement. Secured Party and Secured Party's agent are each of them authorized on behalf of Borrower, as Borrower's agent and attorney-in-fact for such purpose, to complete and sign one or more financing statements with respect to any Collateral Security covered by this Security Agreement and to file the same in any appropriate office or place.

Section 15. Applicable Law. THIS SECURITY AGREEMENT SHALL BE CONSTRUED ACCORDING TO THE LAWS OF THE STATE OF TEXAS.

Section 16. Limitation on Agreements. All agreements between Borrower and Secured Party, whether now existing or hereafter arising and whether written or oral, are hereby expressly limited so that in no contingency or event whatsoever, or by whatever cause or reason, shall the amount paid, or agreed to be paid to Secured Party for the payment or performance of any covenant or obligation contained herein or in by other document evidencing, securing or pertaining to the Obligation or the Collateral Security, exceed the maximum amount permissible under applicable usury law. If from any circumstances whatsoever fulfillment of any provision hereof or of any of such other documents, at the time performance of such provisions shall be due, shall involve transcending the limit of validity prescribed by usury law, then, ipso facto, the obligation to be fulfilled shall be reduced to the limit of such validity, and if from any such circumstance Secured Party shall ever receive as interest or otherwise an amount which would exceed the highest lawful rate, such amount which would be excessive interest shall be added to the Collateral Security, to be held, applied and invested and released to Borrower as provided in this Security Agreement. All sums paid or agreed to be paid to Secured Party for the use, forbearance or detention of any indebtedness of Borrower to Secured Party arising hereunder shall, to the extent permitted by applicable usury law, be amortized, prorated, allocated and spread throughout the full term of this Security Agreement until performance or payment in full of all Obligation so that the actual rate of interest on account of such indebtedness in uniform throughout the term thereof.

Section 17. Further Assurances. Borrower covenants that it shall deliver any and all such further documents, instruments and agreements as Secured Party may reasonably require to give effect to the provisions of this Security Agreement, all in form and substance reasonably satisfactory to Secured Party.

Section 18. Cumulative Remedies. All rights, powers and remedies of Secured Party under this Security Agreement and any and all other documents, instruments and agreements relating thereto are cumulative and not exclusive and shall be in addition to any other rights, powers or remedies provided by law or equity. No limitations or qualification on any right, power, or remedy of Secured Party any other document, instrument or agreement regardless of any conflict between any of the

obligations of Borrower under different documents, instruments or agreements such conflict shall be resolved by permitting Secured Party to enforce the provisions which are more favorable to Secured Party, unless it is otherwise expressly stated in one such document, instrument or agreement that it supersedes or qualifies such other documents, instruments or agreements.

Section 19. Counterparts. This Security Agreement may be executed in any number of counterparts and by different parties in separate counterparts, each of which when which counterparts taken together shall constitute but one and the same instrument.

EXECUTED AND DELIVERED as of the date and year first above written.

BORROWER:

TEXAS PHARMACEUTICALS, INC., a Texas corporation

BY: _____
NAME: _____
TITLE: _____

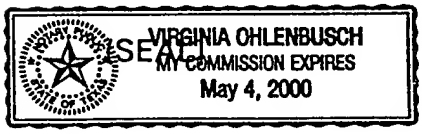
SECURED PARTY:

_____
NICHOLAS BACHYNSKY

STATE OF TEXAS §
§
COUNTY OF BEXAR §

BEFORE ME, the undersigned authority, on this day personally appeared NICHOLAS BACHYNSKY known to me to be the person whose name is subscribed to the foregoing instrument, and acknowledged to me that he executed the same for the purposes and consideration therein expressed.

GIVEN UNDER MY HAND AND SEAL OF OFFICE, this the 5th day of March, 1998.



Virginia Ohlenbusch
Notary Public Signature

Virginia Ohlenbusch
Notary Printed Name

Commission Expires: 5-4-2000

STATE OF TEXAS §
§
COUNTY OF _____ §

BEFORE ME, the undersigned authority, on this day personally appeared JAMES J. NAPLES, President of TEXAS PHARMACEUTICALS, INC., a Texas corporation, known to me to be the person whose name is subscribed to the foregoing instrument, and acknowledged to me that he executed the same for the purposes and consideration therein expressed and in the capacity therein stated, as the act and deed of said corporation.

GIVEN UNDER MY HAND AND SEAL OF OFFICE, this the 10th day of March, 1998.

Patty Hamilton
Notary Public Signature

PATTY HAMILTON
Notary Printed Name

Commission Expires: 11-9-98

Warrant #W001 to Purchase 500,000 shares of Common Stock ($0.01 par value)

WARRANT OF TEXAS PHARMACEUTICALS, INC., A TEXAS CORPORATION

THIS WARRANT OF TEXAS PHARMACEUTICALS, INC., A TEXAS CORPORATION (this "Warrant") certifies that, for value received, the Registered Owner is entitled, subject to the terms and conditions of this Warrant, until the expiration date, to purchase the stated number of shares of the Common Stock, par value $0.01 (the "Common Stock") of TEXAS PHARMACEUTICALS, INC., a Texas corporation (the "Corporation") from the Corporation at the purchase price shown below, on delivery of this Warrant to the Corporation with the exercise form duly executed and payment of the purchase price (in cash or other consideration acceptable to the Corporation) for each share purchased.

REGISTERED OWNER:	Nicholas Bachynsky, 701 W. 14th Street, Texarkana, Texas 75501.
PURCHASE PRICE:	At par.
EXPIRATION DATE:	3:00 P.M., December 31, 1999, unless sooner terminated under this Warrant.

TERMS

1. Corporation's Covenants as to Common Stock. Shares deliverable on the exercise of this Warrant will, at delivery, be fully paid and non-assessable, free from taxes, liens and charges with respect to their purchase. The Corporation will take any necessary steps to assure that the par value per share of the Common Stock is at all times equal to or less than the then current Warrant purchase price per share of the Common Stock issuable pursuant to this Warrant. The Corporation shall at all times reserve and hold available sufficient shares of Common Stock to satisfy all purchase rights of outstanding options and warrants.

2. Method of Exercise. The purchase rights represented by this Warrant are exercisable solely by the Registered Owner in whole at any time. This Warrant does not, prior to exercise, entitle the Registered Owner to any voting rights or other rights as a stockholder of the Corporation, or to any other rights whatsoever except the rights herein expressed. No dividends or distributions are payable or will accrue on this Warrant or the shares available for purchase hereunder until this Warrant is exercised.

3. Transfer. This Warrant is not transferable. The Corporation shall not recognize any purported attempt to transfer this Warrant by Registered Owner or any other person or authority.

4. Recognition of Registered Owner. The Corporation shall treat the Registered Owner as the person exclusively entitled to receive notices and otherwise to exercise rights hereunder.

5. Effect of Certain Events. If the Corporation, by stock dividend, split, reverse split, reclassification of shares, or otherwise, changes as a whole the outstanding Common Stock into a different number of class of shares, then:

   a. the number and class of shares so changed will, for the purposes of this Warrant, replace the shares outstanding immediately prior to the change; and

   b. the Warrant purchase price in effect, and the number of shares available for purchase under this Warrant, immediately prior to the date upon which the change becomes effective, shall be proportionately adjusted (the price to the nearest cent). Irrespective of any change in the Warrant purchase price or the number of shares purchasable under this or any other Warrant of like tenor, the Warrants theretofore or thereafter issued may continue to express the Warrant purchase price per share and the number of shares available for purchase as the Warrant purchase price per share and the number of shares available for purchase were expressed in the Warrants when initially issued.

6. Notice of Adjustment. On the happening of an event requiring an adjustment of the Warrant purchase price or the shares available for purchase hereunder, the Corporation shall forthwith give written notice to the Registered Owner stating the adjusted Warrant purchase price and the adjusted number and kind of securities or other property available for purchase hereunder resulting from the event and setting forth in reasonable detail the method of calculation and the facts upon which the calculation is based. The Board of Directors of the Corporation, acting in good faith, shall determine the calculation.

7. Notice and Effect of Dissolution. In case a voluntary or involuntary dissolution, liquidation, or winding up of the Corporation is at any time proposed, the Corporation shall give written notice to the Registered Owner at least thirty (30) days in advance of such event, if possible. Such notice shall contain (a) the date on which the transaction is to take place; (b) the record date as of which holders of Common Stock will be entitled to receive distributions as a result of the transaction; (c) a brief description of the transaction; (d) a brief description of the distributions to be made to holders of Common Stock as a result of the transaction; and (e) an estimate of the fair value of the distribution. On the date of the transaction, if it actually occurs, this Warrant and all rights hereunder will terminate if this Warrant has not been exercised by the Registered Owner.

8. Notices. Notices shall be given by first class mail, postage prepaid, addressed to the registered owner at the address shown above or other address as may be hereafter provided to the Corporation. No notice to warrant holders is required except as herein specified.

TEXAS PHARMACEUTICALS, INC., a Texas corporation

BY: _____
NAME: JAMES J. NAPLES
TITLE: PRESIDENT
DATE: 3/6/98

EXERCISE FORM

[To be executed by the Registered Owner to exercise the Warrant]

The undersigned hereby surrenders and delivers this Warrant to TEXAS PHARMACEUTICALS, INC., a Texas corporation, together with the cash payment of $5,000.00 (or other consideration acceptable to Corporation) for the purchase of 500,000 shares of Common Stock or such other number of shares as shall be equal to fifty percent (50%) of the total outstanding shares of all classes of stock in TEXAS PHARMACEUTICALS, INC., a Texas corporation.

[Please sign exactly as name appears on Warrant]

NICHOLAS BACHYNSKY

Taxpayer ID No. _____

Date: _____ BY: _____

SCHEDULE 1 TO ASSIGNMENT

INVENTION

This invention provides a medical method for: (1) prevention of life threatening hypothermia; (2) enhancing magnetic resonance spectroscopy and positron emission tomographic metabolic imaging; and (3) treatment of resistant neoplastic and infectious disease by concurrent administration of dinitrophenol [or other mitochondrial thermoregulatory uncoupling agents, e.g., carbonylcyanide m-chorophenylhydrazone (CCCP), carbonylcyanide-p-trifluoromethoxy-phenylhydrazone (FCCP), recombinant brown fat type protein, or lipid proton ionophores] and respiratory oxygen, intravenous fluids, anti-platelet drugs, as needed cooling, and specific metabolic, activating cytokines [e.g., recombinant tumor necrosis factor (TNF), interferons, etc.], hormones (e.g., glucagon), and other medications to control and focally enhance the mitochondrial uncoupling effects.

The present invention avoids the use of labor intensive, complex hyperthermia equipment, including invasive extracorporeal perfusion, with its associated thermal gradient toxicity problems to interposed normal tissues, inherent to all therapeutic methods of delivering heat from the outside-in. A new use(s)/method of generating intracellular oxygen derived free radicals, and heating from within the cell has been discovered for dinitrophenol (or other oxidative phosphorylation uncouplers) in prevention of cold injury, and treatment of free radical-thermosensitive parasites (e.g., Echinococcus), bacteria (e.g., Borrelia burgdorferi), lipid enveloped viruses (e.g., HIV), and neoplasia (e.g., gastric adenocarcinoma). It has further been discovered that cataracts, induced by dinitrophenol in the treatment of chronic obesity, can be prevented by concomitant administration of a variety of free radical scavenging agents, including tocopherol, ascorbic acid, and beta-carotene.

Briefly, the present invention is a new use(s)/method of inducing increased, intracellular free radical flux and hyperthermia, including the procedure of administrating dinitrophenol to patients in doses sufficient to denature and inactivate targeted biologic systems. Concurrent administration of tissue selective activating hormones, biologicals or drugs permits greater enhancement of the therapeutic index, while physiologic gain cooling, fluids, respiratory oxygen, and monitoring procedures permit safe therapeutic control. The figure on the attached page depicts an example use(s)/methodology of this process in an algorithm.

ATTORNEY REPRESENTATION AGREEMENT

RE: Assignment of Invention and Related Rights by NICHOLAS BACHYNSKY ("Seller") to TEXAS PHARMACEUTICALS, INC., A TEXAS CORPORATION ("Buyer"), concerning a novel use and method of inducing intracellular hyperthermia and free radical flux through the use of dinitrophenol and other mitochondrial uncoupling agents in the treatment of infectious and malignant disease.

1. REPRESENTATION. The legal instruments involved in the above-referenced sale of invention and related rights have been prepared for and on behalf of Buyer by GOODE, CASSEB & JONES, a Professional Corporation, Attorneys at Law ("Goode, Casseb & Jones"). The undersigned acknowledges that Goode, Casseb & Jones has acted only as counsel to Buyer, and has not, in any manner, undertaken to assist or render legal advice to the undersigned with respect to this transaction, the subject matter of the transaction, or with respect to any of the documents or instruments being executed in connection therewith. The undersigned further acknowledges that he is aware that he may retain his own legal counsel to advise him regarding the transaction and/or to review and render advice concerning any of the documents or instruments being executed in connection therewith and has in fact sought such advice from Robert White, Attorney at Law.

2. DOCUMENT REVIEWED. The undersigned hereby acknowledges receiving and reading a copy of this Attorney Representation Agreement and by the undersigned's signature affirms the acknowledgment of the undersigned to the accuracy of the above statements and the undersigned's agreement thereto.

Nicholas Bachynsky * See 3 below

NICHOLAS BACHYNSKY
March 4, 1998

3. It is mutually understood that ~~the~~ execution of the stock warrant to this transaction is predicated upon the assumption that the stock issued and outstanding in the Buyer is of one class or series and that the stock warrant entitles Nicholas Bachynsky to ~~more~~ 50% of the authorized shares of the corporation with equal voting rights.

AGREEMENT FOR SALE OF INVENTION AND RELATED RIGHTS

THIS AGREEMENT FOR SALE OF INVENTION AND RELATED RIGHTS (this "Agreement") is made and entered into as of July 20, 1998, by and among, **WOODIE ROY**, whose address for the purposes of this Agreement is c/o 701 W. 14th Street, Texarkana, Bowie County, Texas 75501 (herein, "Seller"), and **TEXAS PHARMACEUTICALS, INC., a Texas corporation**, whose address for the purposes of this Agreement is 701 W. 14th Street, Texarkana, Bowie County, Texas 75501 (herein "Purchaser").

F A C T S

Seller has assisted NICHOLAS BACHYNSKY ("Bachynsky") who, with the financial support of James J. Naples, has been conducting medical research and developing a novel use and method of inducing intracellular hyperthermia and free radical flux through the use of dinitrophenol and other mitochondrial uncoupling agents in the treatment of infectious and malignant disease. Bachynsky and Seller have developed and devised a therapeutic application of dinitrophenol and other mitochondrial uncoupling agents for such purposes. A description of this therapy is attached as Schedule 1 to Exhibit A to this Agreement and the matters described therein and herein are referred to herein, collectively, as the "Invention".

Seller desires to sell Seller's entire right, title and interest in and to such Invention and any and all patents and protections which may hereafter be obtained regarding the Invention (the "Patent Rights"), and Purchaser desires to purchase the Patent Rights, upon the terms and conditions hereinafter set forth. Bachynsky has previously assigned his entire right, title and interest in and to such Invention and any and all patents and protections which may hereafter be obtained regarding the Invention to Purchaser.

NOW, THEREFORE, in consideration of the mutual benefits to be derived and the representations and warranties, conditions and promises herein contained, and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, and intending to be legally bound hereby, the parties agree as follows:

ARTICLE I

GENERAL

1.01 Definitions. Unless otherwise stated in this Agreement, the following terms shall have the indicated meanings (the following definitions to be equally applicable to both the

singular and plural forms of any of the terms herein defined):

"Assets": The assets, rights, interests and properties which are described in Section 1.02 (a) of this Agreement.

"Assignment": The Assignment from Seller, as assignor, to Purchaser, as assignee, in the form attached hereto as Exhibit A.

"Closing": The consummation of the purchase and sale contemplated by this Agreement.

"Closing Date": Tuesday, July 21, 1998 at 11:00 A.M., San Antonio, Texas time, or such other date and time upon which the parties may agree.

"Invention": Seller's invention of a novel use and method of inducing intracellular hyperthermia and free radical flux through the use of dinitrophenol and other mitochondrial uncoupling agents in the treatment of infectious and malignant disease, as more fully set forth in Schedule 1 to the form of Assignment attached hereto as Exhibit A.

"Non-Competition Agreement": The Non-Competition Agreement by and between Seller and Purchaser in the form attached hereto as Exhibit B.

"Patent Rights": The Invention, all of Seller's rights thereunder and therein, all existing and future patent applications relating to the Invention, all patents issued with respect to the Invention, all patents to be issued with respect to the Invention, all renewals or extensions or continuations of patents or patent applications with respect to the Invention, all causes of action relating to any use of the Invention and all international rights of priority with respect to said Invention and all rights to file further applications for patent or patent-like protections for said Invention.

"Purchase Price": The price to be paid by Purchaser to Seller in consideration for the sale by Seller and Purchase by Purchaser of the Assets.

"Records": All of Seller's books, records, papers and instruments of whatever nature and wherever located that relate to the Patent Rights or which are required or necessary in order for Purchaser to fully utilize the economic benefits of the Patent Rights and Invention.

"Stock Warrant" means the Stock Warrant to be tendered by Purchaser to Seller as a portion of the Purchase Price, in the form as set forth on Exhibit C attached hereto and made a part hereof for all purposes.

"Transaction": The sale and purchase of the Assets, assignment and assumption of certain rights and interests, and performance of the covenants, in each case as contemplated by this Agreement.

1.02. Agreement To Purchase and Sell.

(a) On and subject to the terms and conditions of this Agreement, Seller agrees to sell, convey, transfer, assign and deliver to Purchaser, and Purchaser agrees to purchase from Seller, the Invention, Patent Rights and Records.

(b) Seller agrees to enter into and be bound by the Non-Competition Agreement.

(c) Seller agrees to indemnify and hold harmless Purchaser in accordance with the terms of this Agreement.

1.03. Purchase Price. TEN DOLLARS ($10.00) and other good and valuable consideration, as described below.

1.04. Payment of Purchase Price. The Purchase Price shall be payable to Seller by Purchaser as follows:

(a) On or before the Closing Date, James J. Naples has paid in excess of the sum of $165,000.00 in research and testing fees to the Cancer Therapy and Research Center in San Antonio, Texas, and to research laboratories in Syracuse, New York, to or for the benefit of Seller and for other purposes related to such research and testing and for development of the patent application covering the Invention. It is understood and agreed that Purchaser is presently entitled to a credit against the cash consideration payable to Seller by virtue of these cash payments or obligations incurred by James J. Naples to or for the benefit of Seller and/or the Invention prior to the date of this Agreement. Payments were made by James J. Naples prior to the date of this Agreement, and prior to the date of incorporation of Purchaser, in anticipation of this Agreement to fund the costs of research and development of the Invention.

(b) Prior to the Closing Date and to the incorporation of Purchaser, James J. Naples has, from time to time, advanced monies for the benefit of Seller; it is understood and agreed that Purchaser is presently entitled to a credit against the cash consideration payable to Seller by virtue of these cash payments or obligations incurred by James J. Naples to or for the benefit of Seller prior to the date of this Agreement.

(c) On the Closing Date, Purchaser will deliver to Seller a stock warrant authorizing Seller to purchase, for par value of $0.01, 250,000 shares of common stock in Purchaser, being twenty-five percent (25%) of the total issued and outstanding stock in

Purchaser, in the form and upon the terms set forth in Exhibit C.

1.05. No Assumption of Liabilities. By purchase of the Assets, Purchaser takes the assets free of any claims, liens or interests of third parties.

1.06 No Proration of Taxes; Offset. If any taxes of any kind are assessed against any of the Assets, Seller will pay such sums to the appropriate taxing authorities when due, prior to becoming delinquent, shall indemnify Purchaser for all such sums and, in addition to the indemnities hereinafter made, does give and grant to Purchaser an offset against all sums owing and unpaid under the Promissory Note for any amounts owed by Seller which Seller fails to pay.

1.07 Instruments of Transfer; Further Assurances. In order to consummate the Transaction, on the Closing Date the Seller shall deliver to Purchaser an executed and acknowledged, where applicable, original of (a) the Assignment, covering all of the Assets; and (b) the Non-Competition Agreement. At the Closing, and at all times thereafter as may be necessary, Seller agrees to execute and deliver to Purchaser such other instruments or transfers as may be reasonably necessary to vest in Purchaser good and indefeasible title to the Assets and to comply with the purposes and intent of this Agreement.

ARTICLE II

REPRESENTATIONS AND WARRANTIES

2.01. Representations and Warranties of Seller. Seller hereby represents and warrants to Purchaser that the following matters are true and correct on the date of this Agreement and will be true and correct through the Closing Date and thereafter, as if made on and as of that date:

(a) This Agreement constitutes the legal, valid and binding obligation of Seller, enforceable in accordance with its terms; no person or entity other than Seller has any interest in or ownership of the Invention as of the date of this Agreement other than equitable claims of Purchaser and/or James J. Naples by virtue of sums advanced to fund the costs of research and development of the Invention.

(b) Seller has good and indefeasible title to the Assets, free and clear of all liens and claims of third parties and no third party has any right to acquire the Assets superior to Purchaser.

(c) There are no claims, actions, suits or proceedings pending or threatened against Seller which involve any of the

Assets.

(d) Seller has complied in all respects with all applicable laws, ordinances, regulations, statutes, rules and restrictions relating to the Assets, or any part thereof.

(e) There is no fact known to Seller which has specific application to this Transaction or the Assets which could have a material adverse effect on the Assets, the ability of Purchaser obtaining a patent on the Invention, the title of Purchaser in and to the Assets from and after the Closing or any other matter which would adversely impact Purchaser in connection with the Assets.

(f) Seller may execute, deliver and perform this Agreement without the necessity of Seller obtaining any consent, approval, authorization or waiver or giving notice or otherwise, except for such consents, approvals, authorizations, waivers and notices which have been obtained and are unconditional and such notices which have been given.

(g) Seller has not incurred any trade payables which have not been disclosed to Purchaser and shall pay or otherwise satisfy all other claims and liabilities relating to the Assets incurred through the Closing Date. **SELLER AGREES AND DOES HEREBY INDEMNIFY AND HOLD PURCHASER HARMLESS FROM AND AGAINST ALL CLAIMS, LOSSES, DEMANDS, DAMAGES, LIABILITIES, COSTS AND EXPENSES RESULTING FROM OR RELATING TO ANY CLAIM MADE AGAINST PURCHASER ARISING FROM SELLER'S BREACH OF THIS AGREEMENT OR ANY OF ITS TERMS, SUCH AGREEMENT TO SURVIVE THE CLOSING OR ANY TERMINATION OF THIS AGREEMENT.**

2.02 Representations and Warranties of Purchaser. Purchaser represents and warrants to Seller that the following are true and correct on the date of this Agreement and will be true and correct through the Closing Date, as if made on and as of that date:

(a) This Agreement and the Stock Warrant constitute the legal, valid and binding obligations of Purchaser, enforceable in accordance with their terms.

(b) Purchaser may execute, deliver and perform this Agreement without the necessity of Purchaser obtaining any consent, approval, authorization or waiver or giving notice or otherwise, except for such consents, approvals, authorizations, waivers and notices which have been obtained and are unconditional and such notices which have been given.

(c) Purchaser may execute, deliver and perform the Stock Warrant without the necessity of Purchaser obtaining any consent, approval, authorization or waiver or giving notice or otherwise, except such of the foregoing which have been given.

ARTICLE III

CONDITIONS OF CLOSING

3.01. Conditions Imposed by Purchaser. The obligations of Purchaser to consummate the purchase and sale under this Agreement are subject to the satisfaction of the following conditions, each of which may be waived in writing by Purchaser:

(a) Seller shall have delivered to Purchaser the duly executed and acknowledged Assignment.

(b) Seller shall have delivered to Purchaser the duly executed and acknowledged the Non-Competition Agreement.

(c) Seller shall have performed the covenants, agreements and obligations necessary to be performed by Seller under this Agreement prior to the Closing Date.

ARTICLE IV

CLOSING DATE

4.01. Closing Date.

(a) Subject to the right of Seller and Purchaser to terminate this Agreement pursuant to Section 5.02. hereof, the Closing for the consummation of the purchase and sale contemplated by this Agreement will, unless another date is agreed to in writing by Seller and Purchaser, take place on the Closing Date.

(b) For all purposes hereof, the term "the Effective Time of Closing" shall occur upon the delivery to Purchaser of the Assignment and the Non-Competition Agreement and the other documents as contemplated herein on the Closing Date.

ARTICLE V

MISCELLANEOUS

5.01. Further Actions. From time to time, as and when requested by Purchaser or Seller, Seller or Purchaser shall execute and deliver, or cause to be executed and delivered, such documents and instruments and shall take, or cause to be taken, such further or other actions as may be reasonably necessary to effectuate the Transaction and transfer, assign and deliver to Purchaser, or Purchaser's assigns, the Assets (or to evidence the foregoing) and to consummate and to effect the other transactions expressly required to be performed by Seller hereunder.

5.02. No Broker. Seller and Purchaser represent and

warrant to the other that they have no obligation or liability to any broker or finder by reason of the transactions which are the subject of this Agreement. Each party agrees to indemnify the other party against, and to hold the other harmless from, at all times after the date hereof, any and all liabilities and expenses (including without limitation legal fees) resulting from, related to or arising out of any claim by any person for brokerage commissions or finder's fees, or rights to similar compensation, on account of services purportedly rendered on behalf of Seller or Purchaser, as the case may be, in connection with this Agreement or the transactions contemplated hereby.

5.03. Expenses. Except as otherwise specifically provided herein, Seller and Purchaser shall each bear their own legal fees, accounting fees and other costs and expenses with respect to the negotiation, execution and the delivery of this Agreement and the consummation of the transactions hereunder.

5.04. Entire Agreement. This Agreement and the Exhibits hereto are intended by the parties as a final expression of the entire agreement between Seller and Purchaser with respect to the transactions contemplated by this Agreement and supersede all prior oral or written agreements, arrangements or understandings with respect thereto.

5.05. Descriptive Headings. The descriptive headings of this Agreement are for convenience only and shall not control or affect the meaning or construction of any provision of this Agreement.

5.06. Notices. All notices or other communications which are required or permitted hereunder shall be in writing and shall be delivered either personally or by telegram, telex, telecopy or similar facsimile means, by registered or certified mail (postage prepaid and return receipt requested), or by express courier or delivery service, addressed to the addresses of the parties shown on page 1 of this Agreement or at such other address and number as either party shall have previously designated by written notice given to the other party in the manner hereinabove set forth. Notices shall be deemed given when received, if sent by telegram, telex, telecopy or similar facsimile means (confirmation of such receipt by confirmed facsimile transmission being deemed receipt of communications sent by telex, telecopy or other facsimile means); and when delivered and receipted for (or upon the date of attempted delivery where delivery is refused), if hand-delivered, sent by express courier or delivery service, or sent by certified or registered mail.

5.07. GOVERNING LAW. THIS AGREEMENT SHALL BE GOVERNED BY AND CONSTRUED IN ACCORDANCE WITH THE LAWS OF THE STATE OF TEXAS (OTHER THAN THE CHOICE OF LAW PRINCIPLES THEREOF).

5.08. Waivers and Amendments. Any waiver of any term or condition of this Agreement, or any amendment or supplementation of this Agreement, shall be effective only if in writing. A waiver of any breach or failure to enforce any of the terms or conditions of this Agreement shall not in any way affect, limit or waive a party's rights hereunder at any time to enforce strict compliance thereafter with every term or condition of this Agreement.

5.09. Illegalities. In the event that any provision contained in this Agreement shall be determined to be invalid, illegal or unenforceable in any respect for any reason, the validity, legality and enforceability of any such provision in every other respect and the remaining provisions of this Agreement shall not, at the election of the party for whose benefit the provision exists, be in any way impaired.

5.10. Counterparts. This Agreement may be executed in any number of counterparts, and each such counterpart hereof shall be deemed to be an original instrument, but all such counterparts together shall constitute but one Agreement. Facsimiles of signatures shall be deemed as original signatures.

5.11. Survival; Exclusivity of Remedies. The representations and warranties, covenants and agreements of the parties hereto shall survive the Closing.

5.12 Assignment by Purchaser. Purchaser may assign Purchaser's rights under this Agreement without restriction of any kind. Any assignee of Purchaser's rights hereunder shall succeed to all of the rights, powers, duties, benefits and obligations of Purchaser hereunder.

IN WITNESS WHEREOF, the undersigned have executed this Agreement as of the date first above written.

PURCHASER:

TEXAS PHARMACEUTICALS, INC., a Texas corporation

BY: _____
NAME: JAMES J. NAPLES
TITLE: President

SELLER:

_____ 7-24-91
WOODIE ROY

STATE OF TEXAS §
§
COUNTY OF Bowie §

BEFORE ME, the undersigned authority, on this day personally appeared WOODIE ROY known to me to be the person whose name is subscribed to the foregoing instrument, and acknowledged to me that she executed the same for the purposes and consideration therein expressed.

GIVEN UNDER MY HAND AND SEAL OF OFFICE, this the 24 day of July, 1998.

[SEAL] PATRICIA M. REYNOLDS NOTARY PUBLIC STATE OF TEXAS My Commission Expires 09-09-99

Patricia M. Reynolds
Notary Public Signature

PATRICIA M. REYNOLDS
Notary Printed Name
Commission Expires: 9/9/99

STATE OF TEXAS §
§
COUNTY OF Bowie §

BEFORE ME, the undersigned authority, on this day personally appeared JAMES J. NAPLES, President of TEXAS PHARMACEUTICALS, INC., a Texas corporation, known to me to be the person whose name is subscribed to the foregoing instrument, and acknowledged to me that he executed the same for the purposes and consideration therein expressed and in the capacity therein stated, as the act and deed of said corporation.

GIVEN UNDER MY HAND AND SEAL OF OFFICE, this the 24th day of July, 1998.

[SEAL] PATTY HAMILTON Notary Public State of Texas Commission Expires 11-9-98

Patty Hamilton
Notary Public Signature

PATTY HAMILTON
Notary Printed Name
Commission Expires: 11-9-98

EXHIBIT A
TO
AGREEMENT FOR SALE OF INVENTION AND RELATED RIGHTS

ASSIGNMENT

DATE: July 21, 1998

ASSIGNOR: WOODIE ROY
c/o 701 W. 14th Street
Texarkana, Texas 75501

ASSIGNEE: TEXAS PHARMACEUTICALS, INC., a Texas corporation
701 W. 14th Street
Texarkana, Texas 75501

In consideration of Ten Dollars ($10.00) cash in hand paid to me and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, I, WOODIE ROY (hereinafter called "Assignor"), who have made an invention of a novel use and method of inducing intracellular hyperthermia and free radical flux through the use of dinitrophenol and other mitochondrial uncoupling agents in the treatment of infectious and malignant disease, assign, sell, transfer and convey to TEXAS PHARMACEUTICALS, INC., a Texas corporation, whose address is 1314 Main Street, Texarkana, Bowie County, Texas 75501 (hereinafter called "Assignee"), its successors and assigns, Assignor's entire right, title and interest in and to the following rights, interest, and property (hereinafter collectively called the "Rights"):

1. Assignor's invention of uses, methods and therapies of inducing intracellular hyperthermia and free radical flux through the use of dinitrophenol and other mitochondrial uncoupling agents in the treatment of infectious and malignant disease, including without limitation Assignor's rights, powers, interests and title in and to the methods, uses and processes described in Schedule 1 attached to this Assignment,

(collectively, herein called the "Invention").

2. All applications for patent or like protection on said Invention that have been or may in the future be made by Assignor or Assignor's legal representatives, in any and all countries.

3. All patents and like protection that have been or may in the future be granted on said Invention to Assignor or Assignor's legal representatives, in any and all countries of the world.

4. All substitutions for and divisions, continuations, continuations-in-part, renewals, reissues, extensions and the like of said applications and patents and similar rights or grants, including, without limitation, those obtained or permissible under past, present and future law and statutes.

5. All rights of action on account of past, present and future authorized or unauthorized use of said Invention and for infringement of said patents and like protection.

6. The right of Assignee to file in his name disclosure documents, applications for patents and like protection for said Invention in any country and countries in the world.

7. All international rights of priority associated with said Invention, disclosure filings, applications, patents and like protection.

TO HAVE AND TO HOLD the Rights unto the Assignee, its successors and assigns forever, and Assignor does hereby bind himself, his heirs, legal representatives and assigns, to forever WARRANT and DEFEND the title to the Rights unto the said Assignee, its successors and assigns, against any person whomsoever lawfully claiming, or to claim the same, or any part thereof.

Assignor covenants and agrees that Assignor will cooperate with Assignee such that Assignee may enjoy to the fullest extent the benefit of this Assignment. Such cooperation shall include, but not limited to, all of the following:

1. Assignor's prompt execution of all papers that are deemed

necessary or desirable by Assignee to perfect the right, title and interest herein conveyed, and

2. Assignor's prompt execution of all petitions, oaths, specifications, declarations or other papers that are deemed necessary or desirable by Assignee for filing and prosecuting patent applications, for filing and prosecuting substitute, division, continuing, or additional applications in the United States and/or all foreign countries, for filing and prosecuting applications for reissuance or reexamination of letters patent, and for interference proceedings involving and covering any of the Rights, and

3. Assignor's prompt assistance and cooperation, including but not limited to execution of documents and testifying, in the prosecution of legal proceedings involving any of the Rights, including, but not limited to, patent prosecution, interference proceedings, infringement court actions, opposition proceedings, cancellation proceedings, priority contests, unfair competition court actions, trade secret court actions, public use proceedings, slander, license breach and royalty collection proceedings and other legal proceedings.

Assignor warrants that Assignor has the right to make the assignment set forth herein and that no other person or entity has any rights of ownership or claim to the subject matter of this Assignment as of the date of this Assignment. This Assignment is binding upon Assignor, Assignor's heirs, administrators, executors, successors, trustees, devisees and assigns and inures to and for

the benefit of Assignee, its successors and assigns.

EXECUTED effective as of the date first above written and at the time and place indicated below opposite the signature:

WOODIE ROY

Date: 7-24-98

STATE OF TEXAS §
§
COUNTY OF BOWIE §

BEFORE ME, the undersigned authority, on this day personally appeared WOODIE ROY known to me to be the person whose name is subscribed to the foregoing instrument, and acknowledged to me that she executed the same for the purposes and consideration therein expressed.

GIVEN UNDER MY HAND AND SEAL OF OFFICE, this the 24th day of July, 1998.

(SEAL)

PATRICIA M. REYNOLDS
NOTARY PUBLIC
STATE OF TEXAS
My Commission Expires 09-09-99

Patricia M. Reynolds
Notary Public Signature

PATRICIA M. REYNOLDS
Notary Printed Name

Commission Expires: 9/9/99

SCHEDULE 1 TO ASSIGNMENT

INVENTION

This invention provides a medical method for: (1) prevention of life threatening hypothermia; (2) enhancing magnetic resonance spectroscopy and positron emission tomographic metabolic imaging; and (3) treatment of resistant neoplastic and infectious disease by concurrent administration of dinitrophenol [or other mitochondrial thermoregulatory uncoupling agents, e.g., carbonylcyanide m-chorophenylhydrazone (CCCP), carbonylcyanide-p-trifluoromethoxy-phenylhydrazone (FCCP), recombinant brown fat type protein, or lipid proton ionophores] and respiratory oxygen, intravenous fluids, anti-platelet drugs, as needed cooling, and specific metabolic, activating cytokines [e.g., recombinant tumor necrosis factor (TNF), interferons, etc.], hormones (e.g., glucagon), and other medications to control and focally enhance the mitochondrial uncoupling effects.

The present invention avoids the use of labor intensive, complex hyperthermia equipment, including invasive extracorporeal perfusion, with its associated thermal gradient toxicity problems to interposed normal tissues, inherent to all therapeutic methods of delivering heat from the outside-in. A new use(s)/method of generating intracellular oxygen derived free radicals, and heating from within the cell has been discovered for dinitrophenol (or other oxidative phosphorylation uncouplers) in prevention of cold injury, and treatment of free radical-thermosensitive parasites (e.g., Echinococcus), bacteria (e.g., Borrelia burgdorferi), lipid enveloped viruses (e.g., HIV), and neoplasia (e.g., gastric adenocarcinoma). It has further been discovered that cataracts, induced by dinitrophenol in the treatment of chronic obesity, can be prevented by concomitant administration of a variety of free radical scavenging agents, including tocopherol, ascorbic acid, and beta-carotene.

Briefly, the present invention is a new use(s)/method of inducing increased, intracellular free radical flux and hyperthermia, including the procedure of administrating dinitrophenol to patients in doses sufficient to denature and inactivate targeted biologic systems. Concurrent administration of tissue selective activating hormones, biologicals or drugs permits greater enhancement of the therapeutic index, while physiologic gain cooling, fluids, respiratory oxygen, and monitoring procedures permit safe therapeutic control. The figure on the attached page depicts an example use(s)/methodology of this process in an algorithm.

FOR DIAGNOSIS OR TREATMENT OF INFECTIOUS AND MALIGNANT DISEASE

ORGANISM or MALIGNANCY

PATIENT

TREATMENT EVALUATION

BIOLOGIC CRITERIA

* Confirmed Diagnosis by culture, PCR, or histopathology; specific serology.
* Known Temperature and Heating Time required for inactivation, e.g., Treponema pallidum (syphilis)-41.5°C @ 1 hour; Borrelia burgdorferi (Lyme Disease)-41.5°C @ 1 hour; Echinococcus multilocularis (Hydatid infestation)-41°C @ 15 minutes; HIV, chronically infected (provirus) cells (tissue culture)-42°C @ 10 hours, with recombinant TNF-a, 42°C @ 3 hours. Kaposi's sarcoma, HIV infection in the patient-42°C @ 2 hours/44°C @ 15 minutes.
* Unknown Temperature and Heating Time required for inactivation of neoplasms, or other infectious agents, determined by predictive - assay of biopsy/culture; generally, treatment temperature/time will be decreased due to endogenous uncoupling also occurring in targeted biologic system (except viral).

CLINICAL CRITERIA

* History of cardiac, hepatic, pulmonary renal, CNS, malignant hyperthermia, or endocrine disease, i.e., exclusion of patients-congestive heart failure, severe dysrhythmias; alcoholic or other hepatitis with elevated bilirubin/enzymes; known endocrinopathies of brittle diabetes, pheochromocytoma, etc.; medications known to stimulate the physiologic response of hypermetabolic state and hyperthermia, e.g., vascular constrictors, anticholinergics, calcium channel blocker, etc.
* Pulmonary, renal, hepatic function tests; chest X-ray; CBC with platelet count; Chem profile with Ca^{++}, Mg^{++}, $PO_4^{=}$; exercise-multigated cardiac radionucleotide scan with resting ejection fraction of at least 45%, and no deterioration upon exercise.
* Enhancing or sensitizing agents to increase therapeutic gain, i.e., use of ionizing radiation, chemotherapy, drugs, or biologic modifiers (synergistic or additive).

METHOD PROTOCOL

TREATMENT

* Dinitrophenol, dosage & schedule on "Biologic/Clinical Criteria"; IV (or IM-SC) test dose (1mg/kg) by VO_2 response-1ml O_2/sec=20watts; common IV dosage, 1-5mg/kg, q 1-4 hr, PO 2X greater q 6-12 hr; BMR & heat dissipation modify dose/schedule.
* Other mitochondrial uncoupling agents, increased potency/more localized effect, e.g., FCCP, CCCP, perfluorooctane sulfonamide, SF-6847; long chain fatty acids, and brown fat "thermogin", etc.
* Modulating-controlling agents, tissue specific mediators which modulate substrate turnover rates through Krebs cycle; glucagon, .5-10mg/hr-IV; dopamine(1-10 micrograms/kg/min); insulin-dose based on blood glucose; dobutamine(1-15 micrograms/kg/min); amrinone(5-7.5 micrograms/kg/min); isoproterenol (.5-2 micrograms/min).

BASELINE & MONITORED

* Oxygen consumption/increase, precedes core temperature increase by 4 minutes; prolonged or high risk patient-additional monitoring of tissue oxygenation by gastric pH, NMR, PET or infrared spectroscopy, ear oximetry, blood gas.
* Core temperature, esophageal, rectal, bladder catheter thermistors.
* Cardiac function, continous display of rhythm, rate, blood pressure and respiratory rate; Swan-Ganz catheter for high risk patient.
* Renal output/function, maintain at least 1-1.5ml per kg/hour; observe for possible myoglobinuria and monitor fluid input/output.
* Hepatic function tests, at target temperature; isoenzyme fractionation if tumor lysis is a consideration.
* CNS agitation, anxiety, possible seizure prophylaxis.
* Blood chemistry/electrolytes-glucose, $PO_4^{=}$, serum creatinine.

MANAGEMENT

* Oxygen (100%) @ 4-6 liters/minute via nasal cannula/face mask.
* Heat control with evaporation preventing-water absorbing blankets/plastic liners; cooling control-if needed with tepid H_2O spray and/or fan evaporative loss; use of P.O. propylthiouracil (PTU); Decadron-I.V.
* Intravenous fluids, i.e., .85% Saline, D_5W-$\frac{1}{2}$NS, supplemented with appropriate milliequivalents of K^+, $PO_4^{=}$, Mg^{++}; fluid rate to compensate for evaporative and urinary losses, maintain BP.
* Arrhythmia control, if needed-use of non-negative inotropic, or drugs that cannot cause cardiac decompensation in hypermetabolic state e.g., lidocaine; avoidance of beta blockers and Ca^{++} channel blockers.
* Anxiety, possible seizure control with I.V. valium, thiopental; avoidance of drugs with atropine like effects or major anti-psychotic drugs.

MEDICAL USES

DNP-IV @ 1mg/kg ($2X-VO_2$)

DNP-IV @ 2-5mg/kg q3-6hr for $2X-VO_2$

DIAGNOSIS - Enhancement of NMR, PET, & Near-Infrared Spectroscopy. → Sensitivity increased by enhanced metabolic differences between diseased/normal tissues, i.e., O_2, glucose, fatty acid, ATP, phosphocreatine & specific substrate consumption; lactic acid, free radical production; early diagnosis & predictability of disease treatment parameters/success

THERAPY OF INFECTIOUS & MALIGNANT DISEASE- (dosage/frequency of uncoupling agent will be determined by the specific agent created & use of modulating, enhancing, or other combined therapy drugs.

- → PARASITIC (See Illustrative Example)
- 41.5°C/1 hr (or less) → BACTERIAL (Borrelia burgdorferi)
- 42°C/2 to 8 hrs (or less) → VIRAL (HIV)
- Based on predictive biopsy and use of radiation, chemotherapy or biologic response modifiers → NEOPLASTIC

EXAMPLE

A 52 year old white [redacted] male, hunting dog trainer, pre[redacted]ed with right upper quadrant abdominal pain. History revealed past(24 month old) hepatic "cyst" surgery and treatment with albendazole(only 1 dose was given because of anaphylactic reaction). He denied history of weight loss, pulmonary, cardiac or neurologic disease. Upon physical examination, he had a weight of 198 pounds (90 Kg), height of 5'11", blood pressure 140/80, pulse-76 and regular, respirations 18/minute, and oral temperature of 37.3°C. Laboratory studies, including hepatic, renal, pulmonary and cardiac function tests were normal; complete blood count was unremarkable except for 20% eosinophilia. Ultrasound and nuclear magnetic resonance of the liver revealed 4 (2-3 cm. in diameter) cysts in the mid-right lobe; ELISA serology showed a diagnostic titer specific for Hydatid disease with Echinococcus multilocularis. The patient refused to entertain any additional surgery or albendazole therapy.

After clinical assessment and treatment evaluation, i.e., Echinococcus multilocularis protoscoleces and germinal layers are destroyed at 41°C/15 minutes, whereas liver-hepatocytes withstand temperatures of 42°C to 44°C for known periods of 20 hours and 15 minutes respectively, the patient was given 1 aspirin; 10 mg. diazepam by mouth; and, intravenous fluids of 0.85 normal saline containing 9 millimolar K_2PO_4, 7 milliequivalents of K^+, and 2cc of 50% saturated solution of Mg_2SO_4/liter, were infused at a rate of 12cc/kg/hr. Urine output was maintained at 1cc/kg/hour or greater. Esophageal (optional), rectal and foley (16 gauge) tipped bladder catheter thermistors gave temperature readings every two minutes within 0.1°C. Cardiac rate, rhythm, blood pressure, and repiratory rate sensors were placed and continously displayed on a multichannel monitor. Intravenous glucagon-2mg/hr was infused, with 1 mg given prior to DNP.

The patient was covered with a water absorbing polyethelene lined blanket, and baseline respiratory gas flow/oxygen consumption (VO_2) was determined using a 3 minute bag collection. Five minutes after intravenous administration of 90 mg of dinitrophenol (2% DNP/5% $NaHCO_3$ at 1 mg/kg), and determination that there was no untoward or idiosyncratic reaction, an additional 90 mg of 2,4 dinitrophenol (total of 180mg, 2mg/kg body weight) was infused. Monitored physiologic parameters are shown in the Table below. An additional VO_2 rate was obtained five minutes after the second dose of DNP and the patient was thereafter placed on 100% O_2 via nasal canula. Target core temperature was maintained by occasional exposure of a limb and/or decreasing the glucagon infusion rate to 0.25 mg/hour. After the patient was maintained at a core temperature of 41.3°C for 20 minutes, the treatment was terminated by removing the blanket and permitting evaporative and radiant heat loss to return the body temperature to a normothermic level.

TABLE

Monitored Clinical Data On Mitochondrial Uncoupling Use/Method In Illustrative Example
(Treatment of Hydatid disease-Echinococcus multilocularis)

Time (minutes)	Medication (type & dose)	Resp. Rate-O_2 Consumption (breaths/min)	(ml/min)	Cardiac Rate (beats/min)	Urine Output (total ml)	Core Temp. (°C)	Other (remarks)
-60	I.V. Fluids - .85% NS @ 0.3 L/hour	18	290	78	-	37.1	Fluids @ 10-12cc per kg/hour.
-30	Glucagon-IV Drip @ 2mg/hour	20	-	78	47	37.1	Hepatic Krebs Cycle stimulation.
0	2,4-dinitrophenol-90mg IV in 4.5ml of 5%$NaHCO_3$ (prepared by dissolving 2.3gm DNP(15% H_2O) in 5% $NaHCO_3$-giving 2% solution)	20	-	88	58	37.4	Covered with polyethylene blanket.
2		24	330	92	-	37.8	Increased O_2 consumption precedes temp. elevation.
5	2,4-dinitrophenol-90mg IV in 4.5ml of 5%$NaHCO_3$	26	-	98	-	37.9	
10	Fluids increased to 1.2 L/hour; start O_2	30	680	110	15	39.4	After VO_2 determined 100% O_2 @ 4 L/min via nasal cannula.
20	-	30	-	120	18	40.3	
40	Glucagon -IV Drip decreased to 0.5mg/hr	30	-	138	25	41.4	Lower extremity is partially exposed.
60	Glucagon discontinued	30	-	140	30	41.2	Blanket removed
120	IV fluid discontinued	24	-	100	98	38.4	All thermistors removed

1/ Variations of the above use/method, i.e., protocol evaluation, monitoring, medications/dosages, time & temperature of mitochondrial uncoupling, will be necessitated by clinical and targeted biologic system treatment factors. Such variations for treatment of other parasitic (e.g. Malaria), bacterial (e.g., Lyme, Hansens disease), viral (e.g., HIV) and neoplastic disease will occur to those skilled in the art of medicine, and will be more fully described in the patent application.

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

OCTOBER 16, 2001

PTAS

101863154A

FULBRIGHT & JAWORSKI LLP
DAVID L. FOX
1301 MCKINNEY, SUITE 5100
HOUSTON, TX 77010-3095

UNITED STATES PATENT AND TRADEMARK OFFICE
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

THE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF THE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS AVAILABLE AT THE ASSIGNMENT SEARCH ROOM ON THE REEL AND FRAME NUMBER REFERENCED BELOW.

PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE INFORMATION CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA PRESENT IN THE PATENT AND TRADEMARK ASSIGNMENT SYSTEM. IF YOU SHOULD FIND ANY ERRORS OR HAVE QUESTIONS CONCERNING THIS NOTICE, YOU MAY CONTACT THE EMPLOYEE WHOSE NAME APPEARS ON THIS NOTICE AT 703-308-9723. PLEASE SEND REQUEST FOR CORRECTION TO: U.S. PATENT AND TRADEMARK OFFICE, ASSIGNMENT DIVISION, BOX ASSIGNMENTS, CG-4, 1213 JEFFERSON DAVIS HWY, SUITE 320, WASHINGTON, D.C. 20231.

RECORDATION DATE: 07/21/2000

REEL/FRAME: 012063/0023
NUMBER OF PAGES: 8

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:
ROY, WOODIE

DOC DATE: 07/21/1998

ASSIGNEE:
TEXAS PHARMACEUTICALS, INC.
701 W. 4TH STREET
TEXARKANA, TEXAS 75501

SERIAL NUMBER: 09744622
PATENT NUMBER:
PCT NUMBER: US9916940

FILING DATE:
ISSUE DATE:

TARA WASHINGTON, EXAMINER
ASSIGNMENT DIVISION
OFFICE OF PUBLIC RECORDS

Received ND
OCT 23 2001
Docket: PD1615 US1
Client: Tex Pharmaceuticals
Attorney: PEK

Form PTO-1595
(Rev. 6-93)
OMB No. 0651-0011 (exp. 4/94)

10-16-2001

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

MRD
11-21-00

RECOR

101863154

IEET

To the Honorable Commissioner of Patents and Trademarks:
Please record the attached original documents or copy thereof.

1. Name of conveying party(ies):
Woodie Roy

Additional name(s) of conveying party(ies) attached?
☐ Yes ☒ No

2. Name and address of receiving party(ies):

Name: Texas Pharmaceuticals, Inc.

Internal Address:

Street Address: 701 W. 4th Street

City: Texarkana

State: TX Zip: 75501

3. Nature of Conveyance:

☒ Assignment ☐ Merger

☐ Security Agreement ☐ Change of Name

☐ Other

Execution Date: July 21, 1998

Additional name(s) & address(es) attached?
☐ Yes ☒ No

4. Application number(s) or patent number(s): PCT/US99/16940

If this document is being filed together with a new application, the execution date of the application is:

A. Patent Application No.(s):

B. Patent No.(s)

Additional numbers attached? ☐ Yes ☒ No

5. Name and address of party to whom correspondence concerning document should be mailed:

Name: David L. Fox

Internal Address: Fulbright & Jaworski LLP

Street Address: 1301 McKinney

Suite 5100

City: Houston

State: TX Zip: 77010-3095

6. Total number of applications and patents involved: 2

7. Total fee (37 CFR 3.41): ..... $ 40.00

☒ Enclosed

☐ Authorized to be charged to deposit account

8. Deposit account number:

(Attach duplicate copy of this page if paying by deposit account)

DO NOT USE THIS SPACE

9. Statement and signature.
To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is a true copy of the original document.

David L. Fox
Name of Person Signing

Signature

17 July 2000
Date

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Mail documents to be recorded with required cover sheet information to:
Commissioner of Patents & Trademarks, Box Assignments
Washington, D.C. 20231

EXHIBIT B TO AGREEMENT FOR SALE OF INVENTION AND RELATED RIGHTS

NON-COMPETITION AGREEMENT

THIS NON-COMPETITION AGREEMENT (this "Agreement") dated as of July 21, 1998, is by and between **WOODIE ROY**, whose address for the purposes of this Agreement is c/o 701 W. 14th Street, Texarkana, Bowie County, Texas 75501 (the "Seller") and **TEXAS PHARMACEUTICALS, INC., a Texas corporation**, whose address for the purposes of this Agreement is 701 W. 14th Street, Texarkana, Bowie County, Texas 75501 (the "Purchaser").

R E C I T A L S :

A. Seller and Purchaser have entered into an Agreement For Sale of Invention and Related Rights dated as of July 20, 1998 (the "Sales Agreement") pursuant to which, among other things, Purchaser has agreed to purchase from Seller, and Seller has agreed to sell to Purchaser, certain assets of Seller described therein, including (without limitation) Seller's invention of a use and method of inducing intracellular hyperthermia and free radical flux through the use of dinitrophenol and other mitochondrial uncoupling agents in the treatment of infectious and malignant disease (the "Invention") and all rights of Seller under any and all disclosure documents, patents and patent applications relating thereto in all countries of the world and all other rights related to the Invention (the "Assets").

B. Seller possesses certain confidential information relating to the Invention which is proprietary in nature and which is not and will not be generally disclosed. To induce Purchaser to enter into the Sales Agreement and to purchase Seller's Assets, Seller has agreed to enter into this Agreement to assure Purchaser that Seller will not use Seller's confidential information in a manner which will injure the commercial value of the Invention or the Assets.

NOW, THEREFORE, in consideration of the premises and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Seller and Purchaser hereby covenant and agree as follows:

1. Covenant Not To Compete. Seller hereby covenants that commencing upon the date hereof and continuing until November 1, 2005, Seller shall not, unless acting as an employee or licensee of the Purchaser, own, manage, operate, join, control or participate in, directly or indirectly, or derive any benefits whatever from, or be an officer, director, employee, partner, agent, consultant or shareholder of, any business engaged in any activity that is in "Competition" in any manner whatsoever with the business of Purchaser in the "Specified Geographical Area," and Seller shall

not render assistance or advice to any person, firm or enterprise which is so engaged. For purposes of this paragraph,

(a) "Competition" means the treatment of patients using methods covered by the Invention or otherwise using dinitrophenol or other mitochondrial uncoupling agents; and

(b) "Specified Geographical Area" means the United States of America and any location in any country in which Purchaser holds a patent or patent application upon the Invention or rights to assert patent protection under any international treaty or law.

2. Payments in Consideration of Covenant Not To Compete. In consideration of the covenants of Seller set forth in paragraph 1 above, Purchaser has purchased from Seller the Assets for the consideration set forth in the Sales Agreement.

3. Entire Agreement. This Agreement constitutes the entire agreement between the parties hereto with respect to the subject matter of this Agreement and supersedes and is in full substitution for any and all prior agreements and understandings whether written or oral between said parties relating to the subject matter of this Agreement, except as set forth in the Sales Agreement.

4. Amendment. This Agreement may not be amended or modified in any respect except by an agreement in writing executed by the parties in the same manner as this Agreement.

5. Assignment. This Agreement may be assigned without the consent of Seller in connection with the sale, transfer or other assignment of all or substantially all of the assets acquired by the Purchaser from the Seller under the Sales Agreement.

6. Heirs and Successors. This Agreement shall be binding upon and shall inure to the benefit of and be enforceable by each of the parties and their respective heirs, legal representatives, successors and assigns.

7. Invalid Provisions. If any provision of this Agreement is held to be illegal, invalid or unenforceable under present or future law effective during the term hereof, such provision shall be fully severable. This Agreement shall be construed and enforced as if such illegal, invalid or unenforceable provision had never comprised a part hereof and the remaining portions hereof shall remain in full force and effect and shall not be effected by the illegal, invalid or unenforceable provision or by its severance herefrom. Furthermore, in lieu of such illegal, invalid or unenforceable provision there shall be added automatically as part of this Agreement a provision similar in terms to such illegal, invalid or unenforceable provision as may be possible and be legal, valid and enforceable.

8. Specific Performance. Seller acknowledges that Seller's breach of the provisions of Section 1 of this Agreement will cause irrevocable harm to Purchaser, for which there may be no adequate remedy at law and for which the ascertainment of damages would be difficult. Therefore, Purchaser will be entitled, in addition to, and without having to prove the inadequacy of, other remedies at law (including without limitation damages for prior breaches hereof), to specific performance of this Agreement, as well as injunctive relief (without being required to post bond or other security).

9. Notice. All notices, consents, requests, approvals or other communications in connection with this Agreement and all legal process in regard hereto shall be in writing and shall be deemed validly delivered, if delivered personally or sent by certified mail, postage prepaid. Unless changed by written notice pursuant hereto, the address of each party for the purposes hereof is the address set forth on page 1 of this Agreement. Notice given by mail shall be deemed delivered only when actually received.

10. Descriptive Headings. The descriptive headings of the several sections of this Agreement are inserted for convenience only and shall not control or affect the meaning or construction of any of the provisions hereof.

11. GOVERNING LAW. THIS AGREEMENT SHALL BE GOVERNED BY AND CONSTRUED AND ENFORCED IN ACCORDANCE WITH THE LAWS OF THE STATE OF TEXAS (OTHER THAN THE CHOICE OF LAW PRINCIPLES THEREOF).

IN WITNESS WHEREOF, the parties have duly executed this Non-Competition Agreement as of the date first above written.

SELLER:

7-24-98

WOODIE ROY

PURCHASER:

TEXAS PHARMACEUTICALS, INC., a Texas corporation

BY: _____

NAME: JAMES J. NAPLES

TITLE: President

DATE: 7-24-98

EXHIBIT C TO AGREEMENT FOR SALE OF INVENTION AND RELATED RIGHTS

FORM OF STOCK WARRANT

Warrant #W002 to Purchase 250,000 shares of Common Stock ($0.01 par)

WARRANT OF TEXAS PHARMACEUTICALS, INC., A TEXAS CORPORATION

THIS WARRANT OF TEXAS PHARMACEUTICALS, INC., A TEXAS CORPORATION (this "Warrant") certifies that, for value received, the Registered Owner is entitled, subject to the terms and conditions of this Warrant, until the expiration date, to purchase the stated number of shares of the Common Stock, par value $0.01 (the "Common Stock") of TEXAS PHARMACEUTICALS, INC., a Texas corporation (the "Corporation") from the Corporation at the purchase price shown below, on delivery of this Warrant to the Corporation with the exercise form duly executed and payment of the purchase price (in cash or other consideration acceptable to the Corporation) for each share purchased.

REGISTERED OWNER:	WOODIE ROY, 701 W. 14th Street, Texarkana, Texas 75501.
PURCHASE PRICE:	At par.
EXPIRATION DATE:	3:00 P.M., December 31, 1999, unless sooner terminated under this Warrant.

TERMS

1. Corporation's Covenants as to Common Stock. Shares deliverable on the exercise of this Warrant will, at delivery, be fully paid and non-assessable, free from taxes, liens and charges with respect to their purchase. The Corporation will take any necessary steps to assure that the par value per share of the Common Stock is at all times equal to or less than the then current Warrant purchase price per share of the Common Stock issuable pursuant to this Warrant. The Corporation shall at all times reserve and hold available sufficient shares of Common Stock to satisfy all purchase rights of outstanding options and warrants.

2. Method of Exercise. The purchase rights represented by this Warrant are exercisable solely by the Registered Owner in whole at any time. This Warrant does not, prior to exercise, entitle the Registered Owner to any voting rights or other

rights as a stockholder of the Corporation, or to any other rights whatsoever except the rights herein expressed. No dividends or distributions are payable or will accrue on this Warrant or the shares available for purchase hereunder until this Warrant is exercised.

3. Transfer. This Warrant is not transferable. The Corporation shall not recognize any purported attempt to transfer this Warrant by Registered Owner or any other person or authority.

4. Recognition of Registered Owner. The Corporation shall treat the Registered Owner as the person exclusively entitled to receive notices and otherwise to exercise rights hereunder.

5. Effect of Certain Events. If the Corporation, by stock dividend, split, reverse split, reclassification of shares, or otherwise, changes as a whole the outstanding Common Stock into a different number or class of shares, then:

   a. the number and class of shares so changed will, for the purposes of this Warrant, replace the shares outstanding immediately prior to the change; and

   b. the Warrant purchase price in effect, and the number of shares available for purchase under this Warrant, immediately prior to the date upon which the change becomes effective, shall be proportionately adjusted (the price to the nearest cent). Irrespective of any change in the Warrant purchase price or the number of shares purchasable under this or any other Warrant of like tenor, the Warrants theretofore or thereafter issued may continue to express the Warrant purchase price per share and the number of shares available for purchase as the Warrant purchase price per share and the number of shares available for purchase were expressed in the Warrants when initially issued.

6. Notice of Adjustment. On the happening of an event requiring an adjustment of the Warrant purchase price or the shares available for purchase hereunder, the Corporation shall forthwith give written notice to the Registered Owner stating the adjusted Warrant purchase price and the adjusted number and kind of securities or other property available for purchase hereunder resulting from the event and setting forth in reasonable detail the method of calculation and the facts upon which the calculation is based. The Board of Directors of the Corporation, acting in good faith, shall determine the calculation.

7. Notice and Effect of Dissolution. In case a voluntary or involuntary dissolution, liquidation, or winding up of the Corporation is at any time proposed, the Corporation shall

give written notice to the Registered Owner at least thirty (30) days in advance of such event, if possible. Such notice shall contain (a) the date on which the transaction is to take place; (b) the record date as of which holders of Common Stock will be entitled to receive distributions as a result of the transaction; (c) a brief description of the transaction; (d) a brief description of the distributions to be made to holders of Common Stock as a result of the transaction; and (e) an estimate of the fair value of the distribution. On the date of the transaction, if it actually occurs, this Warrant and all rights hereunder will terminate if this Warrant has not been exercised by the Registered Owner.

8. Notices. Notices shall be given by first class mail, postage prepaid, addressed to the registered owner at the address shown above or other address as may be hereafter provided to the Corporation. No notice to warrant holders is required except as herein specified.

TEXAS PHARMACEUTICALS, INC., a Texas corporation

BY: _____
NAME: James J. Naples
TITLE: President
DATE: 7-24-98

EXERCISE FORM

[To be executed by the Registered Owner to exercise the Warrant]

The undersigned hereby surrenders and delivers this Warrant to TEXAS PHARMACEUTICALS, INC., a Texas corporation, together with the cash payment of ~~$5,000.00~~ $31,580.62 (or other consideration acceptable to Corporation) for the purchase of 250,000 shares of Common Stock or such other number of shares as shall be equal to twenty-five percent (25%) of the total outstanding shares of all classes of stock in TEXAS PHARMACEUTICALS, INC., a Texas corporation.

[Please sign exactly as name appears on Warrant]

WOODIE ROY

Taxpayer ID No. 456-82-3199

Date: 7-24-98

BY: _____

AFFIDAVIT AS TO FACT

THE STATE OF TEXAS *
*
COUNTY OF BOWIE * KNOW ALL MEN BY THESE PRESENTS:

BEFORE ME, the undersigned authority on this day personally appeared WOODIE ROY, a single person, whose address is currently TEXARKANA, TEXAS, being over the age of eighteen (18) years and otherwise fully competent to make this Affidavit, and who, after being by me duly sworn, deposed and stated the following to be true and correct:

"I am a co-inventor of the Invention more particularly described on Schedule 1 to this Affidavit.

I have the status of co-inventor based upon my suggestion to Nicholas Bachynsky that dinitrophenol could be used to induce hyperthermia in patients who have cancer or human immuno-deficiency virus (HIV) and my request that he explore the possibility of this use. I knew that certain malignant tumors and HIV are believed to be sensitive to heat and because of my previous work with Dr. Bachynsky using dinitrophenol in other applications, I knew that one of the properties of dinitrophenol is its ability to induce heat in humans.

I recognize and confirm that Texas Pharmaceuticals, Inc. and/or James J. Naples have expended money to research the viability of this application of dinitrophenol and have done so with the understanding that Texas Pharmaceuticals, Inc. would own the commercial rights to any patent or therapy involving the use of dinitrophenol in the treatment of malignant and infectious diseases.

As set forth in my Assignment of my rights to Texas Pharmaceuticals, Inc., I have conveyed all of my right, title and interest in the use of dinitrophenol as therein described for the sole purpose of vesting in Texas Pharmaceuticals, Inc. such rights. I do not know of anyone, other than Nicholas Bachynsky and Texas Pharmaceuticals, Inc., who has any claim to this invention of which I am co-inventor, whether as an inventor or as an assignee of an inventor.

I understand that each of the statements contained herein will be relied upon by Texas Pharmaceuticals, Inc. in paying to me the Purchase Price described in that certain Agreement for Sale of Invention and Related Rights dated July 20, 1998, between me and Texas Pharmaceuticals, Inc.

Further, I represent that I have examined this Affidavit and the attachment hereto and, to the best of my knowledge and belief, it is true, correct and complete."

EXECUTED as of the 24th day of July, 1998.

AFFIANT:

Woodie E Roy
WOODIE ROY

SUBSCRIBED AND SWORN TO ME BY WOODIE ROY on this 24th day of July, 1998.

[SEAL]

Patricia M. Reynolds
NOTARY PUBLIC, STATE OF TEXAS

PATRICIA M. REYNOLDS
Printed/Typed Name of Notary

My Commission Expires:

9/9/99

PATRICIA M. REYNOLDS
NOTARY PUBLIC
STATE OF TEXAS
My Commission Expires 09-09-99

SCHEDULE 1 TO ASSIGNMENT

INVENTION

This invention provides a medical method for: (1) prevention of life threatening hypothermia; (2) enhancing magnetic resonance spectroscopy and positron emission tomographic metabolic imaging; and (3) treatment of resistant neoplastic and infectious disease by concurrent administration of dinitrophenol [or other mitochondrial thermoregulatory uncoupling agents, e.g., carbonylcyanide m-chorophenylhydrazone (CCCP), carbonylcyanide-p-trifluoromethoxy-phenylhydrazone (FCCP), recombinant brown fat type protein, or lipid proton ionophores] and respiratory oxygen, intravenous fluids, anti-platelet drugs, as needed cooling, and specific metabolic, activating cytokines [e.g., recombinant tumor necrosis factor (TNF), interferons, etc.], hormones (e.g., glucagon), and other medications to control and focally enhance the mitochondrial uncoupling effects.

The present invention avoids the use of labor intensive, complex hyperthermia equipment, including invasive extracorporeal perfusion, with its associated thermal gradient toxicity problems to interposed normal tissues, inherent to all therapeutic methods of delivering heat from the outside-in. A new use(s)/method of generating intracellular oxygen derived free radicals, and heating from within the cell has been discovered for dinitrophenol (or other oxidative phosphorylation uncouplers) in prevention of cold injury, and treatment of free radical-thermosensitive parasites (e.g., Echinococcus), bacteria (e.g., Borrelia burgdorferi), lipid enveloped viruses (e.g., HIV), and neoplasia (e.g., gastric adenocarcinoma). It has further been discovered that cataracts, induced by dinitrophenol in the treatment of chronic obesity, can be prevented by concomitant administration of a variety of free radical scavenging agents, including tocopherol, ascorbic acid, and beta-carotene.

Briefly, the present invention is a new use(s)/method of inducing increased, intracellular free radical flux and hyperthermia, including the procedure of administrating dinitrophenol to patients in doses sufficient to denature and inactivate targeted biologic systems. Concurrent administration of tissue selective activating hormones, biologicals or drugs permits greater enhancement of the therapeutic index, while physiologic gain cooling, fluids, respiratory oxygen, and monitoring procedures permit safe therapeutic control. The figure on the attached page depicts an example use(s)/methodology of this process in an algorithm.

SCHEMATIZED MITOCHONDRIAL UNCOUPLING METHOD FOR DIAGNOSIS OR TREATMENT OF INFECTIOUS AND MALIGNANT DISEASE

ORGANISM or MALIGNANCY

PATIENT

TREATMENT EVALUATION

BIOLOGIC CRITERIA

* Confirmed Diagnosis by culture, PCR, or histopathology; specific serology.
* Known Temperature and Heating Time required for inactivation, e.g., Treponema pallidum (syphilis)-41.5°C @ 1 hour; Borrelia burgdorferi (Lyme Disease)-41.5°C @ 1 hour; Echinococcus multilocularis (Hydatid infestation)-41°C @ 15 minutes; HIV, chronically infected (provirus) cells (tissue culture)-42°C @ 10 hours, with recombinant TNF-a, 42°C @ 3 hours. Kaposi's sarcoma, HIV infection in the patient-42°C @ 2 hours/44°C @ 15 minutes.
* Unknown Temperature and Heating Time required for inactivation of neoplasms, or other infectious agents, determined by predictive - assay of biopsy/culture; generally, treatment temperature/time will be decreased due to endogenous uncoupling also occurring in targeted biologic system (except viral).

CLINICAL CRITERIA

* History of cardiac, hepatic, pulmonary renal, CNS, malignant hyperthermia, or endocrine disease, i.e., exclusion of patients-congestive heart failure, severe dysrhythmias; alcoholic or other hepatitis with elevated bilirubin/enzymes; known endocrinopathies of brittle diabetes, pheochromocytoma, etc.; medications known to stimulate the physiologic response of hypermetabolic state and hyperthermia, e.g., vascular constrictors, anticholinergics, calcium channel blocker, etc.
* Pulmonary, renal, hepatic function tests; chest X-ray; CBC with platelet count; Chem profile with Ca^{++}, Mg^{++}, $PO_4^{=}$; exercise-multigated cardiac radionucleotide scan with resting ejection fraction of at least 45%, and no deterioration upon exercise.
* Enhancing or sensitizing agents to increase therapeutic gain, i.e., use of ionizing radiation, chemotherapy, drugs, or biologic modifiers (synergistic or additive).

METHOD PROTOCOL

TREATMENT

* Dinitrophenol, dosage & schedule on "Biologic/Clinical Criteria"; IV (or IM-SC) test dose (1mg/kg) by VO_2 response-1ml O_2/sec-20watts; common IV dosage, 1-5mg/kg, q 1-4 hr, PO 2X greater q 6-12 hr; BMR & heat dissipation modify dose/schedule.
* Other mitochondrial uncoupling agents, increased potency/more localized effect, e.g., FCCP, CCCP, perfluorooctane sulfonamide, SF-6847; long chain fatty acids, and brown fat "thermogin", etc.
* Modulating-controlling agents, tissue specific mediators which modulate substrate turnover rates through Krebs cycle; glucagon, .5-10mg/hr-IV; dopamine(1-10 micrograms/kg/min); insulin-dose based on blood glucose; dobutamine(1-15 micrograms/kg/min); amrinone(5-7.5 micrograms/kg/min); isoproterenol (.5-2 micrograms/min).

BASELINE & MONITORED

* Oxygen consumption/increase, precedes core temperature increase by 4 minutes; prolonged or high risk patient-additional monitoring of tissue oxygenation by gastric pH, NMR, PET or infrared spectroscopy, ear oximetry, blood gas.
* Core temperature, esophageal, rectal, bladder catheter thermistors.
* Cardiac function, continous display of rhythm, rate, blood pressure and respiratory rate; Swan-Ganz catheter for high risk patient.
* Renal output/function, maintain at least 1-1.5ml per kg /hour; observe for possible myoglobinuria and monitor fluid input/output.
* Hepatic function tests, at target temperature; isoenzyme fractionation if tumor lysis is a consideration.
* CNS agitation, anxiety, possible seizure prophylaxis.
* Blood chemistry/electrolytes-glucose, $PO_4^{=}$, serum creatinine.

MANAGEMENT

* Oxygen (100%) @ 4-6 liters/minute via nasal cannula/face mask.
* Heat control with evaporation preventing-water absorbing blankets/plastic liners; cooling control-if needed with tepid H_2O spray and/or fan evaporative loss; use of P.O. propylthiouracil (PTU); Decadron-I.V.
* Intravenous fluids, i.e., .85% Saline, D_5W-$\frac{1}{2}$NS, supplemented with appropriate milliequivalents of K^+, $PO_4^{=}$, Mg^{++}; fluid rate to compensate for evaporative and urinary losses, maintain BP.
* Arrhythmia control, if needed-use of non-negative inotropic, or drugs that cannot cause cardiac decompensation in hypermetabolic state e.g., lidocaine; avoidance of beta blockers and Ca^{++} channel blockers.
* Anxiety, possible seizure control with I.V. valium, thiopental; avoidance of drugs with atropine like effects or major anti-psychotic drugs.

MEDICAL USES

DNP-IV @ 1mg/kg (2X-VO_2) → DIAGNOSIS - Enhancement of NMR, PET, & Near-Infrared Spectroscopy. → Sensitivity increased by enhanced metabolic differences between diseased/normal tissues, i.e., O_2, glucose, fatty acid, ATP, phosphocreatine & specific substrate consumption; lactic acid, free radical production; early diagnosis & predictability of disease treatment parameters/success.

DNP-IV @ 2-5mg/kg q3-6hr for 2X-VO_2 → THERAPY OF INFECTIOUS & MALIGNANT DISEASE (dosage/frequency of uncoupling agent will be determined by the specific agent treated & use of modulating, enhancing, or other combined therapy drugs.

- → PARASITIC (See Illustrative Example)
- 41.5°C/1 hr (or less) → BACTERIAL (Borrelia burgdorferi)
- 42°C/2 to 8 hrs (or less) → VIRAL (HIV)
- Based on predictive biopsy and use of radiation, chemotherapy or biologic response modifiers → NEOPLASTIC

ILLUSTRATIVE METHOD/USE EXAMPLE [1/]

A 52 year old white [redacted]s male, hunting dog trainer, pre[redacted]ted with right upper quadrant abdominal pain. History revealed past(24 month old) hepatic "cyst" surgery and treatment with albendazole(only 1 dose was given because of anaphylactic reaction). He denied history of weight loss, pulmonary, cardiac or neurologic disease. Upon physical examination, he had a weight of 198 pounds (90 Kg), height of 5'11", blood pressure 140/80, pulse-76 and regular, respirations 18/minute, and oral temperature of 37.3°C. Laboratory studies, including hepatic, renal, pulmonary and cardiac function tests were normal; complete blood count was unremarkable except for 20% eosinophilia. Ultrasound and nuclear magnetic resonance of the liver revealed 4 (2-3 cm. in diameter) cysts in the mid-right lobe; ELISA serology showed a diagnostic titer specific for Hydatid disease with Echinococcus multilocularis. The patient refused to entertain any additional surgery or albendazole therapy.

After clinical assessment and treatment evaluation, i.e., Echinococcus multilocularis protoscoleces and germinal layers are destroyed at 41°C/15 minutes, whereas liver-hepatocytes withstand temperatures of 42°C to 44°C for known periods of 20 hours and 15 minutes respectively, the patient was given 1 aspirin; 10 mg. diazepam by mouth; and, intravenous fluids of 0.85 normal saline containing 9 millimolar K_2PO_4, 7 milliequivalents of K^+, and 2cc of 50% saturated solution of Mg_2SO_4/liter, were infused at a rate of 12cc/kg/hr. Urine output was maintained at 1cc/kg/hour or greater. Esophageal (optional), rectal and foley (16 gauge) tipped bladder catheter thermistors gave temperature readings every two minutes within 0.1°C. Cardiac rate, rhythm, blood pressure, and repiratory rate sensors were placed and continously displayed on a multichannel monitor. Intravenous glucagon-2mg/hr was infused, with 1 mg given prior to DNP.

The patient was covered with a water absorbing polyethelene lined blanket, and baseline respiratory gas flow/oxygen consumption (VO_2) was determined using a 3 minute bag collection. Five minutes after intravenous administration of 90 mg of dinitrophenol (2% DNP/5% $NaHCO_3$ at 1 mg/kg), and determination that there was no untoward or idiosyncratic reaction, an additional 90 mg of 2,4 dinitrophenol (total of 180mg, 2mg/kg body weight) was infused. Monitored physiologic parameters are shown in the Table below. An additional VO_2 rate was obtained five minutes after the second dose of DNP and the patient was thereafter placed on 100% O_2 via nasal canula. Target core temperature was maintained by occasional exposure of a limb and/or decreasing the glucagon infusion rate to 0.25 mg/hour. After the patient was maintained at a core temperature of 41.3°C for 20 minutes, the treatment was terminated by removing the blanket and permitting evaporative and radiant heat loss to return the body temperature to a normothermic level.

TABLE

Monitored Clinical Data On Mitochoodrial Uncoupling Use/Method In Illustrative Example
(Treatment of Hydatid disease-Echinococcus multilocularis)

Time (minutes)	Medication (type & dose)	Resp. Rate-O_2 (breaths/min)	Consumption (ml/min)	Cardiac Rate (beats/min)	Urine Output (total ml)	Core Temp. (°C)	Other (remarks)
-60	I.V. Fluids - .85% NS @ 0.8 L/hour	18	290	78	-	37.1	Fluids @ 10-12cc per kg/hour.
-30	Glucagon-IV Drip @ 2mg/hour	20	-	78	47	37.1	Hepatic Krebs Cycle stimulation.
0	2,4-dinitrophenol-90mg IV in 4.5ml of 5%$NaHCO_3$ (prepared by dissolving 2.3gm DNP(15% H_2O) in 5% $NaHCO_3$-giving 2% solution)	20	-	88	58	37.4	Covered with polyethylene blanket.
2		24	350	92	-	37.8	Increased O_2 consumption precedes temp. elevation.
5	2,4-dinitrophenol-90mg IV in 4.5ml of 5%$NaHCO_3$	26	-	98	-	37.8	
10	Fluids increased to 1.2 L/hour; start O_2	30	630	110	15	39.4	After VO_2 determined 100% O_2 @ 4 L/min via nasal cannula.
20	-	30	-	120	18	40.3	
40	Glucagon -IV Drip decreased to 0.5mg/hr	30	-	138	28	41.4	Lower extremity is partially exposed.
60	Glucagon discontinued	30	-	140	30	41.2	Blanket removed
120	IV fluid discontinued	24	-	100	98	38.4	All thermistors removed

1/ Variations of the above use/method, i.e., protocol evaluation, monitoring, medications/dosages, time & temperature of mitochondrial uncoupling, will be necessitated by clinical and targeted biologic system treatment factors. Such variations for treatment of other parasitic (e.g. Malaria), bacterial (e.g., Lyme, Hansens disease), viral (e.g., HIV) and neoplastic disease will occur to those skilled in the art of medicine, and will be more fully described in the patent application.

GOODE CASSEB JONES
RIKLIN CHOATE & WATSON
A PROFESSIONAL CORPORATION
ATTORNEYS AT LAW

G. WAYNE CHOATE
BOARD CERTIFIED
COMMERCIAL REAL ESTATE LAW
TEXAS BOARD OF LEGAL SPECIALIZATION

2122 NORTH MAIN AVENUE
P.O. BOX 120480
SAN ANTONIO, TEXAS 78212-9680

TELEPHONE
(210) 733-6030
FACSIMILE
(210) 733-0330

JOHN GOODE
(1923-1994)

Sender's E-Mail: choate@goodelaw.com

May 1, 2001

CERTIFIED MAIL, RETURN RECEIPT REQUESTED
NO. 7106 4575 1294 0281 2215

Dr. Nicholas Bachynsky
WERNB Medical Interests
5944 Coral Ridge Drive, Ste. 202
Coral Springs, Fl. 33076

Re: Texas Pharmaceuticals, Inc., a Texas corporation (the "Corporation")

Dear Nick:

Enclosed is a Declaration for Patent Application prepared for submission to the U.S. Patent and Trademark Office in connection with the pending Application for Patent concerning chemically induced intracellular hyperthermia. As the co-inventor of the subject matter of this Application for Patent, your certification of the matters set forth in the enclosed Declaration for Patent Application is necessary to complete this application.

As you may recall, under the terms of the Assignment dated March 4, 1998, executed by you, as co-inventor and assignor, to the Corporation, as assignee, you contracted to promptly execute all declarations or other papers that are deemed necessary by the Corporation for filing and prosecuting patent applications (see page 3, numbered paragraph 2). The enclosed document is deemed necessary by the Corporation for such purpose.

Please sign the enclosed document in the space provided beneath your name and address on page 2 and return to me in the enclosed self-addressed and stamped envelope. Upon receipt, I will forward the same to the Corporation's patent counsel for filing with the U.S. Patent and Trademark Office.

If the signed Declaration for Patent Application is not received in my office on or before May 14, 2001, I will assume that you have declined to execute this document and will proceed to prepare the documents necessary to submit such

Declaration for Patent Application. However, I should advise you that your failure to timely sign and return the enclosed document will result in additional, unnecessary expense to the Corporation for which you may be responsible under the terms of the Assignment.

Please call if you have any questions.

Sincerely,

G. Wayne Choate
For the Firm

GWC/yge
3712-001
Enclosures - as noted

cc: (w/o enclosures): Dr. James Naples, President
Texas Pharmaceuticals, Inc.

Melissa D. Schwaller, Ph.D.
Fulbright & Jaworski, L.L.P.

Declaration for Patent Application	Attorney Docket No.	HO-P01615US1
	First Name Inventor	Nicholas Bachynsky
	COMPLETE IF KNOWN:	
☐ Submitted ☒ Submitted after initial	Application No.	09/744,622
	Filing Date	January 26, 2001
	Group Art Unit	N/A
	Examiner	Not Yet Assigned

As a below named inventor, I hereby declare that:

My residence, mailing address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

CHEMICALLY INDUCED INTRACELLULAR HYPERTHERMIA

The specification of which

☐ is attached hereto

OR

☒ was filed on January 26, 2001

as United States Application No. or PCT International Application No. 09/744,622

and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the National or PCT International filing date of the continuation-in-part.

I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) or 365(b) of any foreign applications(s) for patent or inventor's certificate, or 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate or any PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application(s)

			Priority	Certified	
				YES	NO
US99/16940 (Number)	PCT (Country)	07/27/99 (Filing Date)	☐	☐	☒
(Number)	(Country)	(Filing Date)	☐	☐	☐
(Number)	(Country)	(Filing Date)	☐	☐	☐

☐ Additional prior foreign applications are listed on a supplemental data sheet attached hereto.

I hereby claim the benefit under 35 U.S.C. Section 119(e) of any United States provisional application(s) listed below:

60/094,286 (Application No.)	07/27/98 (Filing Date)
(Application No.)	(Filing Date)
(Application No.)	(Filing Date)

☐ Additional U.S. provisional applications are listed on a supplemental data sheet attached hereto.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of sole or first inventor Nicholas Bachynsky
Residence Coral Springs, Florida
Citizenship USA
Mailing Address 5944 Coral Ridge Drive, #202, Coral Springs, Fl 33076

Full name of second inventor Woodie Roy
Residence Coral Springs, Florida
Citizenship USA
Mailing Address 5944 Coral Ridge Drive, #202, Coral Springs, Fl 33076

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as Express Mail, Airbill No. _____, in an envelope addressed to: Commissioner for Patents, Washington, DC 20231, on the date shown below.

Dated: _____, 2001 Signature: _____ (_____)

AT →

2. Article Number

7106 4575 1294 0281 2215

3. Service Type CERTIFIED MAIL

4. Restricted Delivery? *(Extra Fee)* ☐ Yes

1. Article Addressed to:
DR NICHOLAS BACHYNSKY
WERNB MEDICAL INTERESTS
5944 CORAL RIDGE DRIVE STE 202
CORAL SPRINGS FL 33076

COMPLETE THIS SECTION ON DELIVERY

A. Received by (Please Print Clearly) CLAUDIA UREA B. Date of Delivery 5/8

C. Signature X ☐ Agent ☐ Addressee

D. Is delivery address different from item 1? ☐ Yes
If YES, enter delivery address below: ☐ No

RE: ~~3712-001 5/1/01~~ SENDER: ygc

PS Form 3811, June 2000 Domestic Return Receipt

7106 4575 1294 0281 2215

TO: DR NICHOLAS BACHYNSKY
WERNB MEDICAL INTERESTS
5944 CORAL RIDGE DRIVE STE 202
CORAL SPRINGS FL 33076

SENDER: yge

REFERENCE: 3712-001 5/1/01

PS Form 3800, June 2000

RETURN RECEIPT SERVICE	Postage	~~0.00~~
	Certified Fee	~~0.00~~
	Return Receipt Fee	~~0.00~~
	Restricted Delivery	~~0.00~~
	Total Postage & Fees	

US Postal Service

Receipt for Certified Mail

No Insurance Coverage Provided
Do Not Use for International Mail

POSTMARK OR DATE

GOODE CASSEB JONES
RIKLIN CHOATE & WATSON
A PROFESSIONAL CORPORATION
ATTORNEYS AT LAW

G. WAYNE CHOATE
BOARD CERTIFIED
COMMERCIAL REAL ESTATE LAW
TEXAS BOARD OF LEGAL SPECIALIZATION

2122 NORTH MAIN AVENUE
P.O. BOX 120480
SAN ANTONIO, TEXAS 78212-9680

TELEPHONE
(210) 733-6030
FACSIMILE
(210) 733-0330

JOHN GOODE
(1923-1994)

Sender's E-Mail: choate@goodelaw.com

May 1, 2001

CERTIFIED MAIL, RETURN RECEIPT REQUESTED
NO. 7106 4575 1294 0281 2208

Ms. Woodie Roy
WERNB Medical Interests
5944 Coral Ridge Drive, Ste. 202
Coral Springs, Fl. 33076

Re: Texas Pharmaceuticals, Inc., a Texas corporation (the "Corporation")

Dear Woodie:

Enclosed is a Declaration for Patent Application prepared for submission to the U.S. Patent and Trademark Office in connection with the pending Application for Patent concerning chemically induced intracellular hyperthermia. As the co-inventor of the subject matter of this Application for Patent, your certification of the matters set forth in the enclosed Declaration for Patent Application is necessary to complete this application.

As you may recall, under the terms of the Assignment dated July 21, 1998, executed by you, as co-inventor and assignor, to the Corporation, as assignee, you contracted to promptly execute all declarations or other papers that are deemed necessary by the Corporation for filing and prosecuting patent applications (see page 3, numbered paragraph 2). The enclosed document is deemed necessary by the Corporation for such purpose.

Please sign the enclosed document in the space provided beneath your name and address on page 2 and return to me in the enclosed self-addressed and stamped envelope. Upon receipt, I will forward the same to the Corporation's patent counsel for filing with the U.S. Patent and Trademark Office.

If the signed Declaration for Patent Application is not received in my office on or before May 14, 2001, I will assume that you have declined to execute this document and will proceed to prepare the documents necessary to submit such

Declaration for Patent Application. However, I should advise you that your failure to timely sign and return the enclosed document will result in additional, unnecessary expense to the Corporation for which you may be responsible under the terms of the Assignment.

Please call if you have any questions.

Sincerely,

G. Wayne Choate
For the Firm

GWC/yge
3712-001
Enclosures - as noted

cc: (w/o enclosures): Dr. James Naples, President
Texas Pharmaceuticals, Inc.

Melissa D. Schwaller, Ph.D.
Fulbright & Jaworski, L.L.P.

Declaration for Patent Application	Attorney Docket No.	HO-P01615US1
	First Name Inventor	Nicholas Bachynsky
	COMPLETE IF KNOWN:	
☐ Submitted ☒ Submitted after initial	Application No.	09/744,622
	Filing Date	January 26, 2001
	Group Art Unit	N/A
	Examiner	Not Yet Assigned

As a below named inventor, I hereby declare that:

My residence, mailing address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

CHEMICALLY INDUCED INTRACELLULAR HYPERTHERMIA

The specification of which

☐ is attached hereto

OR

☒ was filed on January 26, 2001

as United States Application No. or PCT International Application No. 09/744,622

and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the National or PCT International filing date of the continuation-in-part.

I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) or 365(b) of any foreign applications(s) for patent or inventor's certificate, or 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate or any PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application(s)

			Priority	Certified	
				YES	NO
US99/16940 (Number)	PCT (Country)	07/27/99 (Filing Date)	☐	☐	☒
(Number)	(Country)	(Filing Date)	☐	☐	☐
(Number)	(Country)	(Filing Date)	☐	☐	☐

☐ Additional prior foreign applications are listed on a supplemental data sheet attached hereto.

I hereby claim the benefit under 35 U.S.C. Section 119(e) of any United States provisional application(s) listed below:

60/094,286 (Application No.)	07/27/98 (Filing Date)
(Application No.)	(Filing Date)
(Application No.)	(Filing Date)

☐ Additional U.S. provisional applications are listed on a supplemental data sheet attached hereto.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of sole or first inventor Nicholas Bachynsky
Residence Coral Springs, Florida
Citizenship USA
Mailing Address 5944 Coral Ridge Drive, #202, Coral Springs, Fl 33076

Full name of second inventor Woodie Roy
Residence Coral Springs, Florida
Citizenship USA
Mailing Address 5944 Coral Ridge Drive, #202, Coral Springs, Fl 33076

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as Express Mail, Airbill No. _____, in an envelope addressed to: Commissioner for Patents, Washington, DC 20231, on the date shown below.

Dated: _____, 2001 Signature: _____ (_____)

AY →

2. Article Number

7106 4575 1294 0281 2208

3. Service Type **CERTIFIED MAIL**

4. Restricted Delivery? *(Extra Fee)* ☐ Yes

1. Article Addressed to:

MS WOODIE ROY
WERNB MEDICAL INTERESTS
5944 CORAL RIDGE DRIVE SUITE 202
CORAL SPRINGS FLORIDA 33076

COMPLETE THIS SECTION ON DELIVERY

A. Received by (Please Print Clearly) B. Date of Delivery

C. Signature

X ☐ Agent ☐ Addressee

D. Is delivery address different from item 1? ☐ Yes
If YES, enter delivery address below: ☐ No

RE: ~~3712-001 5/1/01~~ SENDER: ~~yge 5/1/01~~

PS Form 3811, June 2000 Domestic Return Receipt

7106 4575 1294 0281 2208

TO: MS WOODIE ROY
WERNB MEDICAL INTERESTS
5944 CORAL RIDGE DRIVE SUITE 202
CORAL SPRINGS FLORIDA 33076

SENDER: yge 5/1/01

REFERENCE: 3712-001 5/1/01

PS Form 3800, June 2000

RETURN RECEIPT SERVICE	Postage	
	Certified Fee	~~0.00~~
	Return Receipt Fee	~~0.00~~
	Restricted Delivery	~~0.00~~
	Total Postage & Fees	~~0.00~~

US Postal Service

Receipt for Certified Mail

No Insurance Coverage Provided
Do Not Use for International Mail

POSTMARK OR DATE

GOODE CASSEB JONES
RIKLIN CHOATE & WATSON
A PROFESSIONAL CORPORATION
ATTORNEYS AT LAW

G. WAYNE CHOATE
BOARD CERTIFIED
COMMERCIAL REAL ESTATE LAW
TEXAS BOARD OF LEGAL SPECIALIZATION

2122 NORTH MAIN AVENUE
P.O. BOX 120480
SAN ANTONIO, TEXAS 78212-0480

TELEPHONE
(210) 733-8030
FACSIMILE
(210) 733-0330

Sender's E-Mail: choate@goodelaw.com

JOHN GOODE
1923-1994

April 29, 2002

VIA OVERNIGHT COURIER: (954) 522-2200
VIA CERTIFIED MAIL/RRR - 7106 4575 1294 0281 9504

Harris K. Solomon
BRINKLEY, McNERNEY, MORGAN, SOLOMON & TATUM, LLP
200 East Las Olas Boulevard
Suite 1900
Fort Lauderdale, Florida 33301-2209

Re: Nicholas Bachynsky and Woodie Roy

Dear Mr. Solomon:

By letter of August 30, 2001, you wrote to me in your capacity as counsel for Nicholas Bachynsky and Woodie Roy. By telephone conversation of April 26, 2002, between you and Dr. James J. Naples, you confirmed that your firm continues to represent Nicholas Bachynsky and Woodie Roy.

On behalf of my client, Texas Pharmaceuticals, Inc., enclosed are:

1. Declaration for Patent Application English Language Declaration, Attorney Docket No. HO-P01615US1, Nicholas Bachynsky, Inventor, Application No. 09/744,622, Filing Date January 26, 2001, for submission after initial filing, for signature by Nicholas Bachynsky and Woodie Roy; and

2. Copies of documents relating to patent filing by Texas Pharmaceuticals, Inc. under Attorney Docket No. HO-P01615WO0/09805783, Application No. US99/16940, dated July 27, 1999, titled "Chemically Induced Intracellular Hyperthermia" as follows:

   a. Transmittal letter to the United States Designed-Elected Office Concerning a Filing Under 35 U.S.C. 371;

   b. Check No. 44358, dated January 26, 2001, payable to Assistant Commissioner for Patents and Trademarks, for $1,335.00, for filing fee

and prepaid overnight courier wrapper. Please also fax a signed copy to me at (210) 733-0330 not later than Monday, May 6, 2002.

If the fully signed Declaration for Patent Application is not received in my office on or before Monday, May 6, 2002, I will assume that your clients have declined to execute this document.

Under cover of my letter dated May 1, 2001, sent by certified mail, return receipt requested, addressed to Nicholas Bachynsky, a Declaration for Patent Application was submitted to him for signature, and under cover of my letter dated May 1, 2001, sent by certified mail, return receipt requested, addressed to Woodie Roy, a Declaration for Patent Application was submitted to her for signature. Although the return receipts (green cards) were received in my office, neither Mr. Bachynsky nor Ms. Roy returned a signed Declaration for Patent Application.

Texas Pharmaceuticals, Inc. has been put to considerable expense in its efforts to obtain a signed Declaration for Patent Application from Mr. Bachynsky and Ms. Roy, despite their clear contractual obligation to cooperate in providing such documentation. Please provide the signed Declaration for Patent Application without delay to avoid further cost to my client. If your clients continue to refuse to cooperate, Texas Pharmaceuticals, Inc. will hold both Bachynsky and Roy financially responsible for the costs and expenses incurred by Texas Pharmaceuticals, Inc. in obtaining this documentation or in proceeding with the patent application process without this documentation.

To facilitate this process, I have forwarded copies of this letter and all enclosed documentation, including the Declaration for Patent Application, to the last known address for Bachynsky and Roy.

Please call if you have any questions.

Sincerely,

G. Wayne Choate
For the Firm

GWC:yge
3712-003
Enclosures - as noted

cc: Texas Pharmaceuticals, Inc. (letter only)

Nicholas Bachynsky
6090 N.W. 66th Street
Parkland, Florida 33067

Certified Mail/RRR - 7106 4575 1294 0281 9511
Via Overnight Courier

Woodie Roy
6090 N.W. 66th Street
Parkland, Florida 33067

Certified Mail/RRR - 7106 4575 1294 0281 9528
Via Overnight Courier

FedEx Ship Manager

- Ship Inside U.S.
- Ship Outside U.S.
- Ship Inside U.S. - French
- Track Shipment
- Cancel Shipment
- Schedule Courier
- Address Book
- Fast Ship Profiles
- Shipping History

- Update Shipping Profile
- Help/FAQs
- Tutorial
- Contact Information

- My Profile
- Go to fedex.com
- Go to My FedEx
- Go to Ship Manager Login

- Order Supplies

Logout

Shipment Tracking

Harris K. Solomon (Atty)

FedEx has processed your shipment shown below. If you have any questions about this shipment, you can email us or contact your customer service representative.

Tracking Number	790400240100
Reference Number	3712-001
Ship Date	04/29/2002
Delivered To	Recept/Frnt desk
Delivery Location	FORT LAUDERDALE FL
Delivery Date/Time	04/30/2002 08:56
Signed For By	M.VENTERA
Service Type	Priority Letter

Scan Activity	Date/Time	Comments
Delivered FORT LAUDERDALE FL	04/30/2002 08:56	
On FedEx vehicle for delivery FORT LAUDERDALE FL	04/30/2002 08:17	
Left FedEx Ramp FORT LAUDERDALE FL	04/30/2002 07:24	
Arrived at FedEx Destination Location FORT LAUDERDALE FL	04/30/2002 07:13	
Arrived at FedEx Ramp FORT LAUDERDALE FL	04/30/2002 06:04	
Left FedEx Sort Facility FORT WORTH TX	04/30/2002 03:38	
Arrived at Sort Facility FORT WORTH TX	04/30/2002 02:19	
Left FedEx Sort Facility FORT WORTH TX	04/30/2002 00:41	
Arrived at FedEx Ramp SAN ANTONIO TX	04/29/2002 23:33	
Left FedEx Ramp SAN ANTONIO TX	04/29/2002 22:39	
Left FedEx Origin Location SAN ANTONIO TX	04/29/2002 21:31	
Picked up by FedEx SAN ANTONIO TX	04/29/2002 18:18	

Return to Shipping History Return to Shipping

• Track Shipments
• Alternate Reference Track
• Email Track
• FedEx InSight
• Custom Critical
• Cargo Track
• FedEx Freight

Related Links
• Signature Proof
• My FedEx
• FedEx Wireless Solutions
• Handheld Track
• FedEx Sidebar
• Print, Bind & Ship
• FedEx Address Checker

Track Shipments
Detailed Results

Woodie Roy

Quick Help

Tracking Number	831696460515
Reference Number	3712-001
Ship Date	04/29/2002
Delivered To	Recipient
Delivery Location	POMPANO BEACH FL
Delivery Date/Time	05/01/2002 12:59
Signed For By	1694656
Service Type	Priority Pak

Tracking Options
- Obtain a Signature Proof of Delivery
- Email these tracking results to one or more recipients
- Track More Shipments

Scan Activity	Date/Time	Comments
Delivered POMPANO BEACH FL	05/01/2002 12:59	No signature required - release waiver on file
Delivered POMPANO BEACH FL	05/01/2002 12:59	No signature required - release waiver on file
On FedEx vehicle for delivery POMPANO BEACH FL	05/01/2002 12:09	
Package status POMPANO BEACH FL	05/01/2002 11:48	Package in FedEx location
Package status POMPANO BEACH FL	05/01/2002 11:21	Package in FedEx location
Package status POMPANO BEACH FL	05/01/2002 06:55	Package in FedEx location
Package status POMPANO BEACH FL	04/30/2002 17:20	Package in FedEx location
Package status POMPANO BEACH FL	04/30/2002 11:06	Package in FedEx location
Delivery attempt POMPANO BEACH FL	04/30/2002 10:43	Incorrect address
On FedEx vehicle for delivery POMPANO BEACH FL	04/30/2002 08:30	
Arrived at FedEx Destination Location POMPANO BEACH FL	04/30/2002 07:54	
Arrived at Sort Facility FORT WORTH TX	04/30/2002 02:19	
Left FedEx Ramp SAN ANTONIO TX	04/29/2002 22:39	

Email Your Detailed Tracking Results

Enter your email (optional), up to three email addresses as recipients, add your message, and click on Send Email.

From
To
To
To

- Track Shipments
- Alternate Reference Track
- Email Track
- FedEx InSight
- Custom Critical
- Cargo Track
- FedEx Freight

Related Links
- Signature Proof
- My FedEx
- FedEx Wireless Solutions
- Handheld Track
- FedEx Sidebar
- Print, Bind & Ship
- FedEx Address Checker

Track Shipments
Detailed Results

Nicholas Backynsky

Quick Help

Tracking Number	831696460490
Reference Number	3712-001
Ship Date	04/29/2002
Delivered To	Recipient
Delivery Location	POMPANO BEACH FL
Delivery Date/Time	05/01/2002 12:59
Signed For By	1694656
Service Type	Priority Pak

Tracking Options
- Obtain a Signature Proof of Delivery
- Email these tracking results to one or more recipients
- Track More Shipments

Scan Activity	Date/Time	Comments
Delivered POMPANO BEACH FL	05/01/2002 12:59	No signature required - release waiver on file
Delivered POMPANO BEACH FL	05/01/2002 12:59	No signature required - release waiver on file
On FedEx vehicle for delivery POMPANO BEACH FL	05/01/2002 12:09	
Package status POMPANO BEACH FL	05/01/2002 11:48	Package in FedEx location
Package status POMPANO BEACH FL	05/01/2002 06:55	Package in FedEx location
Package status POMPANO BEACH FL	04/30/2002 17:19	Package in FedEx location
Package status POMPANO BEACH FL	04/30/2002 11:06	Package in FedEx location
Delivery attempt POMPANO BEACH FL	04/30/2002 10:43	Incorrect address
On FedEx vehicle for delivery POMPANO BEACH FL	04/30/2002 08:30	
Arrived at FedEx Destination Location POMPANO BEACH FL	04/30/2002 07:54	
Left FedEx Ramp FORT LAUDERDALE FL	04/30/2002 07:23	
Arrived at FedEx Ramp FORT LAUDERDALE FL	04/30/2002 06:04	
Left FedEx Sort Facility FORT WORTH TX	04/30/2002 03:38	

Email Your Detailed Tracking Results
Enter your email (optional), up to three email addresses as recipients, add your message, and click on **Send Email.**

From
To
To
To

INVENTOR DECLARATION

Attorney Docket No. 985783(P016115US0)

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled "Chemically Induced Intracellular Hyperthermia", the specification of which

(check one) ☒ is attached hereto.

☐ was filed on as Application Serial No. or PCT international application No. [and was amended on _____ (if applicable)

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, § 1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, § 119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below any foreign application for patent or inventor's certificate, or of any PCT international application having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)			Priority Claimed	
(Number)	(Country)	(Day/Month/Year Filed)	☐ Yes	☐ No
(Number)	(Country)	(Day/Month/Year Filed)	☐ Yes	☐ No
(Number)	(Country)	(Day/Month/Year Filed)	☐ Yes	☐ No

I hereby claim the benefit under Title 35, United States Code § 119(e) of any United States provisional application(s) listed below:

(Application Serial No.) (Filing Date)

(Application Serial No.) (Filing Date)

I hereby claim the benefit under Title 35, United States Code §120 of any United States application(s), or § 365(b) of any PCT international application designating the United States of America, listed below and insofar as the subject matter of each of the claims of this application is not disclosed in the prior U.S. or PCT international application in the manner provided by the first paragraph of Title 35, U.S.C. §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations §1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application.

(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)
(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

NB

Full Name of Sole or First Inventor	Inventor's Signature	Date
Nicholas Bachynsky		7-24-98
Residence		**Citizenship**
Texarkana, Texas		U.S.
Post Office Address		
Same as above		

Full Name of Second Inventor	Inventor's Signature	Date
Woodie Roy		7-24-98
Residence		**Citizenship**
		U.S.
Post Office Address		
Same as above		

Full Name of Third Inventor	Inventor's Signature	Date
Residence		**Citizenship**
Post Office Address		

Full Name of Fourth Inventor	Inventor's Signature	Date
Residence		**Citizenship**
Post Office Address		

Full Name of Fifth Inventor	Inventor's Signature	Date
Residence		**Citizenship**
Post Office Address		

Full Name of Sixth Inventor	Inventor's Signature	Date
Residence		**Citizenship**
Post Office Address		

Full Name of Seventh Inventor	Inventor's Signature	Date
Residence		**Citizenship**
Post Office Address		

Full Name of Eighth Inventor	Inventor's Signature	Date
Residence		**Citizenship**
Post Office Address		

INVENTOR DECLARATION

Attorney Docket No. 985783(P016/15US0)

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled "Chemically Induced Intracellular Hyperthermia", the specification of which

(check one) ☒ is attached hereto.

☐ was filed on as Application Serial No. or PCT international application No. [and was amended on _____ (if applicable)

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

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I hereby claim foreign priority benefits under Title 35, United States Code, § 119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below any foreign application for patent or inventor's certificate, or of any PCT international application having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)			Priority Claimed	
(Number)	(Country)	(Day/Month/Year Filed)	☐ Yes	☐ No
(Number)	(Country)	(Day/Month/Year Filed)	☐ Yes	☐ No
(Number)	(Country)	(Day/Month/Year Filed)	☐ Yes	☐ No

I hereby claim the benefit under Title 35, United States Code § 119(e) of any United States provisional application(s) listed below:

(Application Serial No.) (Filing Date)

(Application Serial No.) (Filing Date)

I hereby claim the benefit under Title 35, United States Code §120 of any United States application(s), or § 365(b) of any PCT international application designating the United States of America, listed below and insofar as the subject matter of each of the claims of this application is not disclosed in the prior U.S. or PCT international application in the manner provided by the first paragraph of Title 35, U.S.C. §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations §1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application.

(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)
(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full Name of Sole or First Inventor	Inventor's Signature	Date
Nicholas Bachynsky	Nicholas Bachynsky	7-24-98
Residence: Texarkana, Texas		Citizenship: U.S.
Post Office Address: Same as above		

Full Name of Second Inventor	Inventor's Signature	Date
Woodie Roy	Woodie E. Roy	7-24-98
Residence		Citizenship: U.S.
Post Office Address: Same as above		

Full Name of Third Inventor	Inventor's Signature	Date
Residence		Citizenship
Post Office Address		

Full Name of Fourth Inventor	Inventor's Signature	Date
Residence		Citizenship
Post Office Address		

Full Name of Fifth Inventor	Inventor's Signature	Date
Residence		Citizenship
Post Office Address		

Full Name of Sixth Inventor	Inventor's Signature	Date
Residence		Citizenship
Post Office Address		

Full Name of Seventh Inventor	Inventor's Signature	Date
Residence		Citizenship
Post Office Address		

Full Name of Eighth Inventor	Inventor's Signature	Date
Residence		Citizenship
Post Office Address		

ASSIGNMENT

DATE: March 4, 1998

ASSIGNOR: NICHOLAS BACHYNSKY
701 W. 14th Street
Texarkana, Texas 75501

ASSIGNEE: TEXAS PHARMACEUTICALS, INC., a Texas corporation
701 W. 14th Street
Texarkana, Texas 75501

In consideration of Ten Dollars ($10.00) cash in hand paid to me and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, I, NICHOLAS BACHYNSKY (hereinafter called "Assignor"), who have made an invention of a novel use and method of inducing intracellular hyperthermia and free radical flux through the use of dinitrophenol and other mitochondrial uncoupling agents in the treatment of infectious and malignant disease, assign, sell, transfer and convey to TEXAS PHARMACEUTICALS, INC., a Texas corporation, whose address is 1314 Main Street, Texarkana, Bowie County, Texas 75501 (hereinafter called "Assignee"), its successors and assigns, Assignor's entire right, title and interest in and to the following rights, interest, and property (hereinafter collectively called the "Rights"):

1. Assignor's invention of uses, methods and therapies of inducing intracellular hyperthermia and free radical flux through the use of dinitrophenol and other mitochondrial uncoupling agents in the treatment of infectious and malignant disease, including without limitation Assignor's rights, powers, interests and title in and to the methods, uses and processes described in Schedule 1 attached to this Assignment, (collectively, herein called the "Invention").

2. All applications for patent or like protection on said Invention that have been

or may in the future be made by Assignor or Assignor's legal representatives, in any and all countries.

3. All patents and like protection that have been or may in the future be granted on said Invention to Assignor or Assignor's legal representatives, in any and all countries of the world.

4. All substitutions for and divisions, continuations, continuations-in-part, renewals, reissues, extensions and the like of said applications and patents and similar rights or grants, including, without limitation, those obtained or permissible under past, present and future law and statutes.

5. All rights of action on account of past, present and future authorized or unauthorized use of said Invention and for infringement of said patents and like protection.

6. The right of Assignee to file in his name disclosure documents, applications for patents and like protection for said Invention in any country and countries in the world.

7. All international rights of priority associated with said Invention, disclosure filings, applications, patents and like protection.

TO HAVE AND TO HOLD the Rights unto the Assignee, its successors and assigns forever, and Assignor does hereby bind himself, his heirs, legal representatives and assigns, to forever WARRANT and DEFEND the title to the Rights unto the said Assignee, its successors and assigns, against any person whomsoever lawfully claiming, or to claim the same, or any part thereof.

Assignor covenants and agrees that Assignor will cooperate with Assignee such that Assignee may enjoy to the fullest extent the benefit of this Assignment. Such cooperation shall include, but not limited to, all of the following:

1. Assignor's prompt execution of all papers that are deemed necessary or desirable by Assignee to perfect the right, title and interest herein conveyed, and

2. Assignor's prompt execution of all petitions, oaths, specifications, declarations

or other papers that are deemed necessary or desirable by Assignee for filing and prosecuting patent applications, for filing and prosecuting substitute, division, continuing, or additional applications in the United States and/or all foreign countries, for filing and prosecuting applications for reissuance or reexamination of letters patent, and for interference proceedings involving and covering any of the Rights, and

3. Assignor's prompt assistance and cooperation, including but not limited to execution of documents and testifying, in the prosecution of legal proceedings involving any of the Rights, including, but not limited to, patent prosecution, interference proceedings, infringement court actions, opposition proceedings, cancellation proceedings, priority contests, unfair competition court actions, trade secret court actions, public use proceedings, slander, license breach and royalty collection proceedings and other legal proceedings.

Assignor warrants that Assignor has the right to make the assignment set forth herein and that no other person or entity has any rights of ownership or claim to the subject matter of this Assignment. This Assignment is binding upon Assignor, Assignor's heirs, administrators, executors, successors, trustees, devisees and assigns and inures to and for the benefit of Assignee, its successors and assigns.

EXECUTED effective as of the date first above written and at the time and place indicated below opposite the signature:

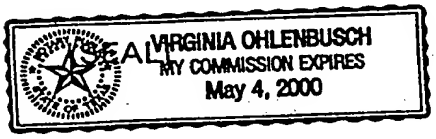
NICHOLAS BACHYNSKY

Date: 3/4/98

STATE OF TEXAS §
§
COUNTY OF BEXAR §

BEFORE ME, the undersigned authority, on this day personally appeared NICHOLAS BACHYNSKY known to me to be the person whose name is subscribed to the foregoing instrument, and acknowledged to me that he executed the same for the purposes and consideration therein expressed.

GIVEN UNDER MY HAND AND SEAL OF OFFICE, this the 5th day of March, 1998.



Virginia Ohlenbusch
Notary Public Signature

Virginia Ohlenbusch
Notary Printed Name

Commission Expires: 5-4-2000

SCHEDULE 1 TO ASSIGNMENT

INVENTION

This invention provides a medical method for: (1) prevention of life threatening hypothermia; (2) enhancing magnetic resonance spectroscopy and positron emission tomographic metabolic imaging; and (3) treatment of resistant neoplastic and infectious disease by concurrent administration of dinitrophenol [or other mitochondrial thermoregulatory uncoupling agents, e.g., carbonylcyanide m-chorophenylhydrazone (CCCP), carbonylcyanide-p-trifluoromethoxy-phenylhydrazone (FCCP), recombinant brown fat type protein, or lipid proton ionophores] and respiratory oxygen, intravenous fluids, anti-platelet drugs, as needed cooling, and specific metabolic, activating cytokines [e.g., recombinant tumor necrosis factor (TNF), interferons, etc.], hormones (e.g., glucagon), and other medications to control and focally enhance the mitochondrial uncoupling effects.

The present invention avoids the use of labor intensive, complex hyperthermia equipment, including invasive extracorporeal perfusion, with its associated thermal gradient toxicity problems to interposed normal tissues, inherent to all therapeutic methods of delivering heat from the outside-in. A new use(s)/method of generating intracellular oxygen derived free radicals, and heating from within the cell has been discovered for dinitrophenol (or other oxidative phosphorylation uncouplers) in prevention of cold injury, and treatment of free radical-thermosensitive parasites (e.g., Echinococcus), bacteria (e.g., Borrelia burgdorferi), lipid enveloped viruses (e.g., HIV), and neoplasia (e.g., gastric adenocarcinoma). It has further been discovered that cataracts, induced by dinitrophenol in the treatment of chronic obesity, can be prevented by concomitant administration of a variety of free radical scavenging agents, including tocopherol, ascorbic acid, and beta-carotene.

Briefly, the present invention is a new use(s)/method of inducing increased, intracellular free radical flux and hyperthermia, including the procedure of administrating dinitrophenol to patients in doses sufficient to denature and inactivate targeted biologic systems. Concurrent administration of tissue selective activating hormones, biologicals or drugs permits greater enhancement of the therapeutic index, while physiologic gain cooling, fluids, respiratory oxygen, and monitoring procedures permit safe therapeutic control. The figure on the attached page depicts an example use(s)/methodology of this process in an algorithm.

SCHEMATIZED MITOCHONDRIAL UNCOUPLING METHOD FOR DIAGNOSIS OF TREATMENT OF INFECTIOUS AND MALIGNANT DISEASE

ORGANISM or MALIGNANCY — PATIENT

TREATMENT EVALUATION

BIOLOGIC CRITERIA

* Confirmed Diagnosis by culture, PCR, or histopathology; specific serology.
* Known Temperature and Heating Time required for inactivation, e.g., Treponema pallidum (syphilis)-41.5°C @ 1 hour; Borrelia burgdorferi (Lyme Disease)-41.5°C @ 1 hour; Echinococcus multilocularis (Hydatid infestation)-41°C @ 15 minutes; HIV, chronically infected (provirus) cells (tissue culture)-42°C @ 10 hours, with recombinant TNF-a, 42°C @ 3 hours. Kaposi's sarcoma, HIV infection in the patient-42°C @ 2 hours/44°C @ 15 minutes.
* Unknown Temperature and Heating Time required for inactivation of neoplasms, or other infectious agents, determined by predictive - assay of biopsy/culture; generally, treatment temperature/time will be decreased due to endogenous uncoupling also occurring in targeted biologic system (except viral).

CLINICAL CRITERIA

* History of cardiac, hepatic, pulmonary renal, CNS, malignant hyperthermia, or endocrine disease, i.e., exclusion of patients-congestive heart failure, severe dysrhythmias; alcoholic or other hepatitis with elevated bilirubin/enzymes; known endocrinopathies of brittle diabetes, pheochromocytoma, etc.; medications known to stimulate the physiologic response of hypermetabolic state and hyperthermia, e.g., vascular constrictors, anticholinergics, calcium channel blocker, etc.
* Pulmonary, renal, hepatic function tests; chest X-ray; CBC with platelet count; Chem profile with Ca^{++}, Mg^{++}, $PO_4^{=}$; exercise-multigated cardiac radionucleotide scan with resting ejection fraction of at least 45%, and no deterioration upon exercise.
* Enhancing or sensitizing agents to increase therapeutic gain, i.e., use of ionizing radiation, chemotherapy, drugs, or biologic modifiers (synergistic or additive).

METHOD PROTOCOL

TREATMENT

* Dinitrophenol, dosage & schedule on "Biologic/Clinical Criteria"; IV (or IM-SC) test dose (1mg/kg) by VO_2 response-1ml O_2/sec-20watts; common IV dosage, 1-5mg/kg, q 1-4 hr, PO 2X greater q 6-12 hr; BMR & heat dissipation modify dose/schedule.
* Other mitochondrial uncoupling agents, increased potency/more localized effect, e.g., FCCP, CCCP, perfluorooctane sulfonamide, SF-6847; long chain fatty acids, and brown fat "thermogin", etc.
* Modulating-controlling agents, tissue specific mediators which modulate substrate turnover rates through Krebs cycle; glucagon, .5-10mg/hr-IV; dopamine(1-10 micrograms/kg/min); insulin-dose based on blood glucose; dobutamine(1-15 micrograms/kg/min); amrinone(5-7.5 micrograms/kg/min); isoproterenol (.5-2 micrograms/min).

BASELINE & MONITORED

* Oxygen consumption/increase, precedes core temperature increase by 4 minutes; prolonged or high risk patient-additional monitoring of tissue oxygenation by gastric pH, NMR, PET or infrared spectroscopy, ear oximetry, blood gas.
* Core temperature, esophageal, rectal, bladder catheter thermistors.
* Cardiac function, continous display of rhythm, rate, blood pressure and respiratory rate; Swan-Ganz catheter for high risk patient.
* Renal output/function, maintain at least 1-1.5ml per kg/hour; observe for possible myoglobinuria and monitor fluid input/output.
* Hepatic function tests, at target temperature; iosoenzyme fractionation if tumor lysis is a consideration.
* CNS agitation, anxiety, possible seizure prophylaxis.
* Blood chemistry/electrolytes-glucose, $PO_4^{=}$, serum creatinine.

MANAGEMENT

* Oxygen (100%) @ 4-6 liters/minute via nasal cannula/face mask.
* Heat control with evaporation preventing water absorbing blankets/plastic liners; cooling control-if needed with tepid H_2O spray and/or fan evaporative loss; use of P.O. propylthiouracil (PTU); Decadron-I.V.
* Intravenous fluids, i.e., .85% Saline, D_5W-½NS, supplemented with appropriate milliequivalents of K^+, $PO_4^{=}$, Mg^{++}; fluid rate to compensate for evaporative and urinary losses, maintain BP.
* Arrhythmia control, if needed-use of non-negative inotropic, or drugs that cannot cause cardiac decompensation in hypermetabolic state e.g., lidocaine; avoidance of beta blockers and Ca^{++} channel blockers.
* Anxiety, possible seizure control with I.V. valium, thiopental; avoidance of drugs with atropine like effects or major anti-psychotic drugs.

MEDICAL USES

DNP-IV @ 1mg/kg (2X-VO_2) → DIAGNOSIS - Enhancement of NMR, PET, & Near-Infrared Spectroscopy. → Sensitivity increased by enhanced metabolic difference between diseased/normal tissues, i.e., O_2, glucose, fatty acid, ATP, phosphocreatine & specific substrate consumption; lactic acid, free radical production; early diagnosis & predictability of disease treatment parameters/success

DNP-IV @ 2-5mg/kg q3-6hr for 2X-VO_2 → THERAPY OF INFECTIOUS & MALIGNANT DISEASE (dosage/frequency of uncoupling agent will be determined by the specific agent treated & use of modulating, enhancing, or other combined therapy drugs

- → PARASITIC (See Illustrative Example)
- 41.5°C/1 hr (or less) → BACTERIAL (Borrelia burgdorferi)
- 42°C/2 to 8 hrs (or less) → VIRAL (HIV)
- Based on predictive biopsy and use of radiation. → NEOPLASTIC

ILLUSTRATIVE METHOD/USE EXAMPLE [1/]

A 52 year old white Swiss male, hunting dog trainer, presented with right upper quadrant abdominal pain. History revealed past(24 month old) hepatic "cyst" surgery and treatment with albendazole(only 1 dose was given because of anaphylactic reaction). He denied history of weight loss, pulmonary, cardiac or neurologic disease. Upon physical examination, he had a weight of 198 pounds (90 Kg), height of 5'11", blood pressure 140/80, pulse-76 and regular, respirations 18/minute, and oral temperature of 37.3°C. Laboratory studies, including hepatic, renal, pulmonary and cardiac function tests were normal; complete blood count was unremarkable except for 20% eosinophilia. Ultrasound and nuclear magnetic resonance of the liver revealed 4 (2-3 cm. in diameter) cysts in the mid-right lobe; ELISA serology showed a diagnostic titer specific for Hydatid disease with Echinococcus multilocularis. The patient refused to entertain any additional surgery or albendazole therapy.

After clinical assessment and treatment evaluation, i.e., Echinococcus multilocularis protoscoleces and germinal layers are destroyed at 41°C/15 minutes, whereas liver-hepatocytes withstand temperatures of 42°C to 44°C for known periods of 20 hours and 15 minutes respectively, the patient was given 1 aspirin; 10 mg. diazepam by mouth; and, intravenous fluids of 0.85 normal saline containing 9 millimolar K_2PO_4, 7 milliequivalents of K^+, and 2cc of 50% saturated solution of Mg_2SO_4/liter, were infused at a rate of 12cc/kg/hr. Urine output was maintained at 1cc/kg/hour or greater. Esophageal (optional), rectal and foley (16 gauge) tipped bladder catheter thermistors gave temperature readings every two minutes within 0.1°C. Cardiac rate, rhythm, blood pressure, and repiratory rate sensors were placed and continously displayed on a multichannel monitor. Intravenous glucagon-2mg/hr was infused, with 1 mg given prior to DNP.

The patient was covered with a water absorbing polyethelene lined blanket, and baseline respiratory gas flow/oxygen consumption (VO_2) was determined using a 3 minute bag collection. Five minutes after intravenous administration of 90 mg of dinitrophenol (2% DNP/5% $NaHCO_3$ at 1 mg/kg), and determination that there was no untoward or idiosyncratic reaction, an additional 90 mg of 2,4 dinitrophenol (total of 180mg, 2mg/kg body weight) was infused. Monitored physiologic parameters are shown in the Table below. An additional VO_2 rate was obtained five minutes after the second dose of DNP and the patient was thereafter placed on 100% O_2 via nasal canula. Target core temperature was maintained by occasional exposure of a limb and/or decreasing the glucagon infusion rate to 0.25 mg/hour. After the patient was maintained at a core temperature of 41.3°C for 20 minutes, the treatment was terminated by removing the blanket and permitting evaporative and radiant heat loss to return the body temperature to a normothermic level.

TABLE

Monitored Clinical Data On Mitochondrial Uncoupling Use/Method In Illustrative Example
(Treatment of Hydatid disease-Echinococcus multilocularis)

Time (minutes)	Medication (type & dose)	Resp. Rate-O_2 Consumption (breaths/min)	ml/min	Cardiac Rate (beats/min)	Urine Output (total ml)	Core Temp. (°C)	Other (remarks)
-60	I.V. Fluids - .85% NS @ 0.8 L/hour	18	290	78	-	37.1	Fluids @ 10-12cc per kg/hour.
-30	Glucagon-IV Drip @ 2mg/hour	20	-	78	47	37.1	Hepatic Krebs Cycle stimulation.
0	2,4-dinitrophenol-90mg IV in 4.5ml of 5%$NaHCO_3$	20	-	88	58	37.4	Covered with polyethylene blanket.
2	[prepared by dissolving 2.3gm DNP(15% H_2O) in 5% $NaHCO_3$-giving 2% solution)	24	350	92	-	37.8	Increased O_2 consumption precedes temp. elevation.
5	2,4-dinitrophenol-90mg IV in 4.5ml of 5%$NaHCO_3$	26	-	98	-	37.8	
10	Fluids increased to 1.2 L/hour; start O_2	30	680	110	15	39.4	After VO_2 determined 100% O_2 @ 4 L/min via nasal cannula.
20	-	30	-	120	18	40.3	
40	Glucagon -IV Drip decreased to 0.5mg/hr	30	-	138	28	41.4	Lower extremity is partially exposed.
60	Glucagon discontinued	30	-	140	30	41.2	Blanket removed
120	IV fluid discontinued	24	-	100	98	38.4	All thermistors removed

1/ Variations of the above use/method, i.e., protocol evaluation, monitoring, medications/dosages, time & temperature of mitochondrial uncoupling, will be necessitated by clinical and targeted biologic system treatment factors. Such variations for treatment of other parasitic (e.g. Malaria), bacterial (e.g., Lyme, Hansens disease), viral (e.g., HIV) and neoplastic disease will occur to those skilled in the art of medicine, and will be more fully described in the patent application.

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SEPTEMBER 29, 2000

FULBRIGHT & JAWORSKI LLP
DAVID L. FOX
1301 MCKINNEY
SUITE 5100
HOUSTON, TX 77010-3095

PTAS Received

OCT 1 0 2000

Docket: P01615US0
Client: Texas Pharmaceutical
Attorney: DLF

101434965A

UNITED STATES PATENT AND TRADEMARK OFFICE
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

THE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF THE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS AVAILABLE AT THE ASSIGNMENT SEARCH ROOM ON THE REEL AND FRAME NUMBER REFERENCED BELOW.

PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE INFORMATION CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA PRESENT IN THE PATENT AND TRADEMARK ASSIGNMENT SYSTEM. IF YOU SHOULD FIND ANY ERRORS OR HAVE QUESTIONS CONCERNING THIS NOTICE, YOU MAY CONTACT THE EMPLOYEE WHOSE NAME APPEARS ON THIS NOTICE AT 703-308-9723. PLEASE SEND REQUEST FOR CORRECTION TO: U.S. PATENT AND TRADEMARK OFFICE, ASSIGNMENT DIVISION, BOX ASSIGNMENTS, CG-4, 1213 JEFFERSON DAVIS HWY, SUITE 320, WASHINGTON, D.C. 20231.

RECORDATION DATE: 07/24/2000

REEL/FRAME: 010993/0076
NUMBER OF PAGES: 8

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:
BACHYNSKY, NICHOLAS

DOC DATE: 03/04/1998

ASSIGNEE:
TEXAS PHARMACEUTICALS, INC.
701 W. 4TH STREET
TEXARKANA, TEXAS 75501

SERIAL NUMBER: 60094286
PATENT NUMBER:

FILING DATE: 07/27/1998
ISSUE DATE:

TARA WASHINGTON, EXAMINER
ASSIGNMENT DIVISION
OFFICE OF PUBLIC RECORDS

Form PTO-1595
(Rev. 6-93)
OMB No. 0651-0011 (exp. 4/94)

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

08-17-2000

101434965

RECOR[illegible]EET

To the Honorable Commissioner of [illegible]rademarks:
Please record the attached original documents or copy thereof.

1. Name of conveying party(ies):
Nicholas Bachynsky

Additional name(s) of conveying party(ies) attached?
☐ Yes ☒ No

4 MD
7.24.00

2. Name and address of receiving party(ies):

Name: Texas Pharmaceuticals, Inc.

Internal Address:

Street Address: 701 W. 4th Street

City: Texarkana

State: TX Zip: 75501

3. Nature of Conveyance:

☒ Assignment ☐ Merger

☐ Security Agreement ☐ Change of Name

☐ Other

Execution Date: March 4, 1998

Additional name(s) & address(es) attached?
☐ Yes ☒ No

4. Application number(s) or patent number(s): 60/094,286

If this document is being filed together with a new application, the execution date of the application is:

A. Patent Application No.(s):

B. Patent No.(s)

Additional numbers attached? ☐ Yes ☒ No

5. Name and address of party to whom correspondence concerning document should be mailed:

Name: David L. Fox

Internal Address: Fulbright & Jaworski LLP

Street Address: 1301 McKinney

Suite 5100

City: Houston

State: TX Zip: 77010-3095

6. Total number of applications and patents involved: 1

7. Total fee (37 CFR 3.41): ..... $ 40.00

☒ Enclosed

☐ Authorized to be charged to deposit account

8. Deposit account number:

(Attach duplicate copy of this page if paying by deposit account)

DO NOT USE THIS SPACE

9. Statement and signature.
To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is a true copy of the original document.

David L. Fox
Name of Person Signing

Signature

17 July 2000
Date

08/16/2000 MTHAI1 00000273 60094286
01 FC:581 40.00 OP

Total number of pages including cover sheet, attachments, and document: 8

Mail documents to be recorded with required cover sheet information to:
Commissioner of Patents & Trademarks, Box Assignments
Washington, D.C. 20231

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to BOX: ASSIGNMENT; Assistant Commissioner for Patents, Washington, D.C. 20231 on 17 July 2000.
Colby S. Delgado
Signature 17 July 00 Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	§	
Nicholas Bachynsky	§	
Woodie Roy	§	
	§	**Atty. Docket: P01615US0 / 09805783**
Serial No.: 60/094,286	§	
	§	**Group Art Unit: Unknown**
Filed: July 27, 1998	§	
	§	**Examiner: Unknown**
For: CHEMICALLY INDUCED INTRA-CELLULAR HYPERTHERMIA	§	

BOX: ASSIGNMENT
Assistant Commissioner for Patents
Washington, D.C. 20231

TRANSMITTAL LETTER

Dear Sir:

Enclosed for filing in the above-identified provisional application are the following:

- Assignment executed by Nicholas Bachynsky on March 4, 1998 and Recordation Form Coversheet;
- Assignment executed by Woodie Roy on July 21, 1998 and Recordation Form Coversheet;
- Check in the amount of $80.00; and
- Return postcard.

Please charge any additional fees and/or credits to the deposit account of Fulbright & Jaworski L.L.P. under account number 06-2375/09805783, from which the undersigned is authorized to draw. A duplicate of this letter is enclosed for accounting purposes.

Respectfully submitted,

Date: 17 July 2000

David L. Fox, Ph.D.
Reg. No. 40,612

FULBRIGHT & JAWORSKI L.L.P.
1301 McKinney, Suite 5100
Houston, Texas 77010-3095
Phone: 713-651-8231
Facsimile: 713-651-5246

ASSIGNMENT

DATE: July 21, 1998

ASSIGNOR: WOODIE ROY
c/o 701 W. 14th Street
Texarkana, Texas 75501

ASSIGNEE: TEXAS PHARMACEUTICALS, INC., a Texas corporation
701 W. 14th Street
Texarkana, Texas 75501

In consideration of Ten Dollars ($10.00) cash in hand paid to me and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, I, WOODIE ROY (hereinafter called "Assignor"), who have made an invention of a novel use and method of inducing intracellular hyperthermia and free radical flux through the use of dinitrophenol and other mitochondrial uncoupling agents in the treatment of infectious and malignant disease, assign, sell, transfer and convey to TEXAS PHARMACEUTICALS, INC., a Texas corporation, whose address is 1314 Main Street, Texarkana, Bowie County, Texas 75501 (hereinafter called "Assignee"), its successors and assigns, Assignor's entire right, title and interest in and to the following rights, interest, and property (hereinafter collectively called the "Rights"):

1. Assignor's invention of uses, methods and therapies of inducing intracellular hyperthermia and free radical flux through the use of dinitrophenol and other mitochondrial uncoupling agents in the treatment of infectious and malignant disease, including without limitation Assignor's rights, powers, interests and title in and to the methods, uses and processes described in Schedule 1 attached to this Assignment, (collectively, herein called the "Invention").

2. All applications for patent or like protection on said Invention that have been or may in the future be made by Assignor or Assignor's legal representatives, in any and all countries.

3. All patents and like protection that have been or may in the future be granted on said Invention to Assignor or Assignor's legal representatives, in any and all countries of the world.

4. All substitutions for and divisions, continuations, continuations-in-part, renewals, reissues, extensions and the like of said applications and patents and similar rights or grants, including, without limitation, those obtained or permissible under past, present and future law and statutes.

5. All rights of action on account of past, present and future authorized or unauthorized use of said Invention and for infringement of said patents and like protection.

6. The right of Assignee to file in his name disclosure documents, applications for patents and like protection for said Invention in any country and countries in the world.

7. All international rights of priority associated with said Invention, disclosure filings, applications, patents and like protection.

TO HAVE AND TO HOLD the Rights unto the Assignee, its successors and assigns forever, and Assignor does hereby bind himself, his heirs, legal representatives and assigns, to forever WARRANT and DEFEND the title to the Rights unto the said Assignee, its successors and assigns, against any person whomsoever lawfully claiming, or to claim the same, or any part thereof.

Assignor covenants and agrees that Assignor will cooperate with Assignee such that Assignee may enjoy to the fullest extent the benefit of this Assignment. Such cooperation shall include, but not limited to, all of the following:

1. Assignor's prompt execution of all papers that are deemed necessary or desirable by Assignee to perfect the right, title and

interest herein conveyed, and

2. Assignor's prompt execution of all petitions, oaths, specifications, declarations or other papers that are deemed necessary or desirable by Assignee for filing and prosecuting patent applications, for filing and prosecuting substitute, division, continuing, or additional applications in the United States and/or all foreign countries, for filing and prosecuting applications for reissuance or reexamination of letters patent, and for interference proceedings involving and covering any of the Rights, and

3. Assignor's prompt assistance and cooperation, including but not limited to execution of documents and testifying, in the prosecution of legal proceedings involving any of the Rights, including, but not limited to, patent prosecution, interference proceedings, infringement court actions, opposition proceedings, cancellation proceedings, priority contests, unfair competition court actions, trade secret court actions, public use proceedings, slander, license breach and royalty collection proceedings and other legal proceedings.

Assignor warrants that Assignor has the right to make the assignment set forth herein and that no other person or entity has any rights of ownership or claim to the subject matter of this Assignment as of the date of this Assignment. This Assignment is binding upon Assignor, Assignor's heirs, administrators, executors, successors, trustees, devisees and assigns and inures to and for the benefit of Assignee, its successors and assigns.

EXECUTED effective as of the date first above written and at the time and place indicated below opposite the signature:

Woodie Roy
WOODIE ROY

Date: 7-24-98

STATE OF TEXAS §
§
COUNTY OF BOWIE §

BEFORE ME, the undersigned authority, on this day personally appeared WOODIE ROY known to me to be the person whose name is subscribed to the foregoing instrument, and acknowledged to me that she executed the same for the purposes and consideration therein expressed.

GIVEN UNDER MY HAND AND SEAL OF OFFICE, this the 24th day of July, 1998.

(SEAL)

PATRICIA M. REYNOLDS
NOTARY PUBLIC
STATE OF TEXAS
My Commission Expires 09-09-99

Patricia M. Reynolds
Notary Public Signature

PATRICIA M. REYNOLDS
Notary Printed Name

Commission Expires: 9/9/99

SCHEDULE 1 TO ASSIGNMENT

INVENTION

This invention provides a medical method for: (1) prevention of life threatening hypothermia; (2) enhancing magnetic resonance spectroscopy and positron emission tomographic metabolic imaging; and (3) treatment of resistant neoplastic and infectious disease by concurrent administration of dinitrophenol [or other mitochondrial thermoregulatory uncoupling agents, e.g., carbonylcyanide m-chorophenylhydrazone (CCCP), carbonylcyanide-p-trifluoromethoxy-phenylhydrazone (FCCP), recombinant brown fat type protein, or lipid proton ionophores] and respiratory oxygen, intravenous fluids, anti-platelet drugs, as needed cooling, and specific metabolic, activating cytokines [e.g., recombinant tumor necrosis factor (TNF), interferons, etc.], hormones (e.g., glucagon), and other medications to control and focally enhance the mitochondrial uncoupling effects.

The present invention avoids the use of labor intensive, complex hyperthermia equipment, including invasive extracorporeal perfusion, with its associated thermal gradient toxicity problems to interposed normal tissues, inherent to all therapeutic methods of delivering heat from the outside-in. A new use(s)/method of generating intracellular oxygen derived free radicals, and heating from within the cell has been discovered for dinitrophenol (or other oxidative phosphorylation uncouplers) in prevention of cold injury, and treatment of free radical-thermosensitive parasites (e.g., Echinococcus), bacteria (e.g., Borrelia burgdorferi), lipid enveloped viruses (e.g., HIV), and neoplasia (e.g., gastric adenocarcinoma). It has further been discovered that cataracts, induced by dinitrophenol in the treatment of chronic obesity, can be prevented by concomitant administration of a variety of free radical scavenging agents, including tocopherol, ascorbic acid, and beta-carotene.

Briefly, the present invention is a new use(s)/method of inducing increased, intracellular free radical flux and hyperthermia, including the procedure of administrating dinitrophenol to patients in doses sufficient to denature and inactivate targeted biologic systems. Concurrent administration of tissue selective activating hormones, biologicals or drugs permits greater enhancement of the therapeutic index, while physiologic gain cooling, fluids, respiratory oxygen, and monitoring procedures permit safe therapeutic control. The figure on the attached page depicts an example use(s)/methodology of this process in an algorithm.

SCHEMATIZED MITOCHONDRIAL UNCOUPLING METHOD FOR DIAGNOSIS OR TREATMENT OF INFECTIOUS & MALIGNANT DISEASE

ORGANISM or MALIGNANCY — PATIENT

TREATMENT EVALUATION

BIOLOGIC CRITERIA

* Confirmed Diagnosis by culture, PCR, or histopathology; specific serology.
* Known Temperature and Heating Time required for inactivation, e.g., Treponema pallidum (syphilis)-41.5°C @ 1 hour; Borrelia burgdorferi (Lyme Disease)-41.5°C @ 1 hour; Echinococcus multilocularis (Hydatid infestation)-41°C @ 15 minutes; HIV, chronically infected (provirus) cells (tissue culture)-42°C @ 10 hours, with recombinant TNF-a, 42°C @ 3 hours. Kaposi's sarcoma, HIV infection in the patient-42°C @ 2 hours/44°C @ 15 minutes.
* Unknown Temperature and Heating Time required for inactivation of neoplasms, or other infectious agents, determined by predictive - assay of biopsy/culture; generally, treatment temperature/time will be decreased due to endogenous uncoupling also occurring in targeted biologic system (except viral).

CLINICAL CRITERIA

* History of cardiac, hepatic, pulmonary renal, CNS, malignant hyperthermia, or endocrine disease, i.e., exclusion of patients-congestive heart failure, severe dysrhythmias; alcoholic or other hepatitis with elevated bilirubin/enzymes; known endocrinopathies of brittle diabetes, pheochromocytoma, etc.; medications known to stimulate the physiologic response of hypermetabolic state and hyperthermia, e.g., vascular constrictors, anticholinergics, calcium channel blocker, etc.
* Pulmonary, renal, hepatic function tests; chest X-ray; CBC with platelet count; Chem profile with Ca^{++}, Mg^{++}, $PO_4^{=}$; exercise-multigated cardiac radionucleotide scan with resting ejection fraction of at least 45%, and no deterioration upon exercise.
* Enhancing or sensitizing agents to increase therapeutic gain, i.e., use of ionizing radiation, chemotherapy, drugs, or biologic modifiers (synergistic or additive).

METHOD PROTOCOL

TREATMENT

* Dinitrophenol, dosage & schedule on "Biologic/Clinical Criteria"; IV (or IM-SC) test dose (1mg/kg) by VO_2 response-1ml O_2/sec=20 watts; common IV dosage, 1-5mg/kg, q 1-4 hr, PO 2X greater q 6-12 hr; BMR & heat dissipation modify dose/schedule.
* Other mitochondrial uncoupling agents, increased potency/more localized effect, e.g., FCCP, CCCP, perfluorooctane sulfonamide, SF-6847; long chain fatty acids, and brown fat "thermogin", etc.
* Modulating-controlling agents, tissue specific mediators which modulate substrate turnover rates through Krebs cycle; glucagon, .5-10mg/hr-IV; dopamine(1-10 micrograms/kg/min); insulin-dose based on blood glucose; dobutamine(1-15 micrograms/kg/min); amrinone(5-7.5 micrograms/kg/min); isoproterenol (.5-2 micrograms/min).

BASELINE & MONITORED

* Oxygen consumption/increase, precedes core temperature increase by 4 minutes; prolonged or high risk patient-additional monitoring of tissue oxygenation by gastric pH, NMR, PET or infrared spectroscopy, ear oximetry, blood gas.
* Core temperature, esophageal, rectal, bladder catheter thermistors.
* Cardiac function, continous display of rhythm, rate, blood pressure and respiratory rate; Swan-Ganz catheter for high risk patient.
* Renal output/function, maintain at least 1-1.5ml per kg/hour; observe for possible myoglobinuria and monitor fluid input/output.
* Hepatic function tests, at target temperature; isoenzyme fractionation if tumor lysis is a consideration.
* CNS agitation, anxiety, possible seizure prophylaxis.
* Blood chemistry/electrolytes-glucose, $PO_4^{=}$, serum creatinine.

MANAGEMENT

* Oxygen (100%) @ 4-6 liters/minute via nasal cannula/face mask.
* Heat control with evaporation prevent water absorbing blankets/plastic liner cooling control-if needed with cepid H spray and/or fan evaporative loss; use P.O. propylthiouracil (PTU); Decadron-I
* Intravenous fluids, i.e., .85% Saline, D_5W-$\frac{1}{2}$NS, supplemented with appropriat milliequivalents of K^+, $PO_4^{=}$, Mg^{++}; fl rate to compensate for evaporative and urinary losses, maintain BP.
* Arrhythmia control, if needed-use of n negative inotropic, or drugs that cann cause cardiac decompensation in hyperm bolic state e.g., lidocaine; avoidance beta blockers and Ca^{++} channel blocker
* Anxiety, possible seizure control with I.V. valium, thiopental; avoidance of drugs with atropine like effects or ma anti-psychotic drugs.

MEDICAL USES

DNP-IV @ 1mg/kg (2X-VO_2) → DIAGNOSIS - Enhancement of NMR, PET, & Near-Infrared Spectroscopy. → Sensitivity increased by enhanced metabolic differen between diseased/normal tissues, i.e., O_2, glucose, f acid, ATP, phosphocreatine & specific substrate cons ion; lactic acid, free radical production; early dia & predictability of disease treatment parameters/su

DNP-IV @ 2-5mg/kg 9J-6hr for 2X-VO_2 → THERAPY OF INFECTIOUS & MALIGNANT DISEASE (dosage/frequency of uncoupling agent will be determined by the specific agent treated & use of modulating, enhancing, or other combined therapy drugs.

- → PARASITIC (See Illustrative Example)
- 41.5°C/1 hr (or less) → BACTERIAL (Borrelia burgdorferi)
- 42°C/2 to 8 hrs (or less) → VIRAL (HIV)
- Based on predictive biopsy and use of radiation, chemotherapy or biologic response modifiers → NEOPLASTIC

ILLUSTRATIVE METHOD/USE EXAMPLE 2/

A 52 year old white S[redacted] male, hunting dog trainer, presented with right upper quadrant abdominal pain. History revealed past(24 month old) hepatic "cyst" surgery and treatment with albendazole(only 1 dose was given because of anaphylactic reaction). He denied history of weight loss, pulmonary, cardiac or neurologic disease. Upon physical examination, he had a weight of 198 pounds (90 Kg), height of 5'11", blood pressure 140/80, pulse-76 and regular, respirations 18/minute, and oral temperature of 37.3°C. Laboratory studies, including hepatic, renal, pulmonary and cardiac function tests were normal; complete blood count was unremarkable except for 20% eosinophilia. Ultrasound and nuclear magnetic resonance of the liver revealed 4 (2-3 cm. in diameter) cysts in the mid-right lobe; ELISA serology showed a diagnostic titer specific for Hydatid disease with Echinococcus multilocularis. The patient refused to entertain any additional surgery or albendazole therapy.

After clinical assessment and treatment evaluation, i.e., Echinococcus multilocularis protoscoleces and germinal layers are destroyed at 41°C/15 minutes, whereas liver-hepatocytes withstand temperatures of 42°C to 44°C for known periods of 20 hours and 15 minutes respectively, the patient was given 1 aspirin; 10 mg. diazepam by mouth; and, intravenous fluids of 0.85 normal saline containing 9 millimolar K_2PO_4, 7 milliequivalents of K^+, and 2cc of 50% saturated solution of Mg_2SO_4/liter, were infused at a rate of 12cc/kg/hr. Urine output was maintained at 1cc/kg/hour or greater. Esophageal (optional), rectal and foley (16 gauge) tipped bladder catheter thermistors gave temperature readings every two minutes within 0.1°C. Cardiac rate, rhythm, blood pressure, and repiratory rate sensors were placed and continously displayed on a multichannel monitor. Intravenous glucagon-2mg/hr was infused, with 1 mg given prior to DNP.

The patient was covered with a water absorbing polyethelene lined blanket, and baseline respiratory gas flow/oxygen consumption (VO_2) was determined using a 3 minute bag collection. Five minutes after intravenous administration of 90 mg of dinitrophenol (2% DNP/5% $NaHCO_3$ at 1 mg/kg), and determination that there was no untoward or idiosyncratic reaction, an additional 90 mg of 2,4 dinitrophenol (total of 180mg, 2mg/kg body weight) was infused. Monitored physiologic parameters are shown in the Table below. An additional VO_2 rate was obtained five minutes after the second dose of DNP and the patient was thereafter placed on 100% O_2 via nasal canula. Target core temperature was maintained by occasional exposure of a limb and/or decreasing the glucagon infusion rate to 0.25 mg/hour. After the patient was maintained at a core temperature of 41.3°C for 20 minutes, the treatment was terminated by removing the blanket and permitting evaporative and radiant heat loss to return the body temperature to a normothermic level.

TABLE

Monitored Clinical Data On Mitochondrial Uncoupling Use/Method In Illustrative Example
(Treatment of Hydatid disease-Echinococcus multilocularis)

Time (minutes)	Medication (type & dose)	Resp. Rate-O_2 Consumption (breaths/min)	O_2 Consumption (ml/min)	Cardiac Rate (beats/min)	Urine Output (total ml)	Core Temp. (°C)	Other (remarks)
-60	I.V. Fluids - .85% NS @ 0.8 L/hour	18	230	78	-	37.1	Fluids @ 10-12cc per kg/hour.
-30	Glucagon-IV Drip @ 2mg/hour	20	-	75	47	37.1	Hepatic Krebs Cycle stimulation.
0	2,4-dinitrophenol-90mg IV in 4.5ml of 5%$NaHCO_3$	20	-	88	53	37.4	Covered with polyethylene blanket.
2	(prepared by dissolving 2.3gm DNP(15% H_2O) in 5% $NaHCO_3$-giving 2% solution)	24	330	92	-	37.8	Increased O_2 consumption precedes temp. elevation.
5	2,4-dinitrophenol-90mg IV in 4.5ml of 5%$NaHCO_3$	26	-	98	-	37.8	
10	Fluids increased to 1.2 L/hour; start O_2	30	630	110	15	39.4	After VO_2 determined 100% O_2 @ 4 L/min via nasal canula.
20	-	30	-	120	18	40.3	
40	Glucagon -IV Drip decreased to 0.5mg/hr	30	-	136	25	41.4	Lower extremity is partially exposed.
60	Glucagon discontinued	30	-	140	30	41.2	Blanket removed
120	IV fluid discontinued	24	-	100	98	38.4	All thermistors removed

1/ Variations of the above use/method, i.e., protocol evaluation, monitoring, medications/dosages, clue & temperature of mitochondrial uncoupling, will be necessitated by clinical and targeted biologic system treatment factors. Such variations for treatment of other parasitic (e.g. Malaria), bacterial (e.g., Lyme, Hansens disease), viral (e.g., HIV) and neoplastic disease will occur to those skilled in the art of medicine, and will be more fully described in the patent application.

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